DETERMINATION OF ABSOLUTE CONFIGURATION OF SECONDARY ALCOHOLS USING THIN-LAYER CHROMATOGRAPHY

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SUPPORTING INFORMATION

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Reaction Conditions for Table 1, Entries 1-13.

The table below contains reaction conditions for all samples used in Table 1. The protocol listed in the experimental for using parallel reactions in the process of determining absolute configuration was followed for all of the entries.

Entry	Original amount of alcohol (mg/μmol)	$CDCl_3$ added to alcohol vial (μL)	Alcohol solution added to each reaction (μL)	*R*-HBTM solution added to *R*-HBTM reaction (μL)	*S*-HBTM solution added to *S*-HBTM reaction (μL)	iPr_2NEt solution added to each reaction (μL)	$(EtCO)_2O$ solution added to each reaction (μL)	Methanol-d_4 added to quench each reaction (μL)	$CDCl_3$ added to give 500 μL total volume for each reaction (μL)
1	9.1/74	403.8	175.0	131.6	131.6	72.5	67.0	50.0	4.0
2[a]	10.4/60.9	403.8	175.0	108.3	108.3	59.7	55.1	50.0	51.9
3[a]	9.7/58	403.8	175.0	103.1	103.1	56.9	52.5	50.0	62.6
4	8.9/48	300.0	130.0	85.2	85.2	47.2	43.4	50.0	144.2
5	5.1/19	150.0	65.0	33.8	33.8	18.6	17.2	50.0	315.4
6	8.7/40	276.9	120.0	71.2	71.2	39.2	36.2	50.0	183.5
7	6.3/25	184.6	80.0	44.4	44.4	24.6	22.6	50.0	278.4
8	5.7/18	150.0	65.0	32.0	32.0	17.8	16.2	50.0	319.0
9	5.6/17	150.0	65.0	30.2	30.2	16.8	15.4	50.0	322.7
10	7.3/32	196.2	85.0	56.8	56.8	31.4	28.8	50.0	247.8
11	6.6/18	150.0	65.0	32.0	32.0	17.6	16.2	50.0	319.1
12	6.2/18	150.0	65.0	32.0	32.0	17.6	16.2	50.0	319.1
13	5.8/20	150.0	65.0	35.6	35.6	19.6	18.0	50.0	311.7

(a) The peak from methanol-d_4 overlaid a peak from the alcohol used in determining conversion in the crude ^{1}H NMR spectrum. The solution was concentrated under reduced pressure. Then, 500 μL of $CDCl_3$ was added and a second ^{1}H NMR spectrum was taken. Both spectra are included.

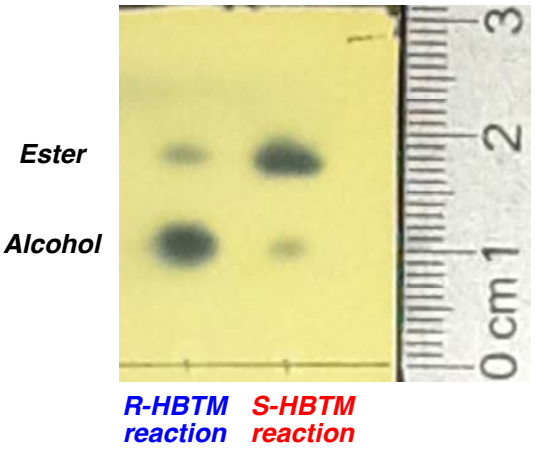
^{1}H NMR spectra were collected for both the *R*-HBTM and the *S*-HBTM crude reaction mixtures. Percent conversion for each reaction was measured according the integrals of each peak after phase correction, line broadening, and automatic baseline correction of all spectra (Formula 1).

Formula 1.

$$\text{Percent Conversion} = \frac{^1\text{H NMR integral}_{\text{ESTER}}}{^1\text{H NMR integral}_{\text{ESTER}} + ^1\text{H NMR integral}_{\text{ALCOHOL}}} \times 100$$

Summary of TLC and ^{1}H NMR Spectral Data, Entries 1-13.

Entry 1. (a) TLC of parallel reactions (b) ^{1}H NMR Spectra of parallel reactions in $CDCl_3$ at 500 MHz.



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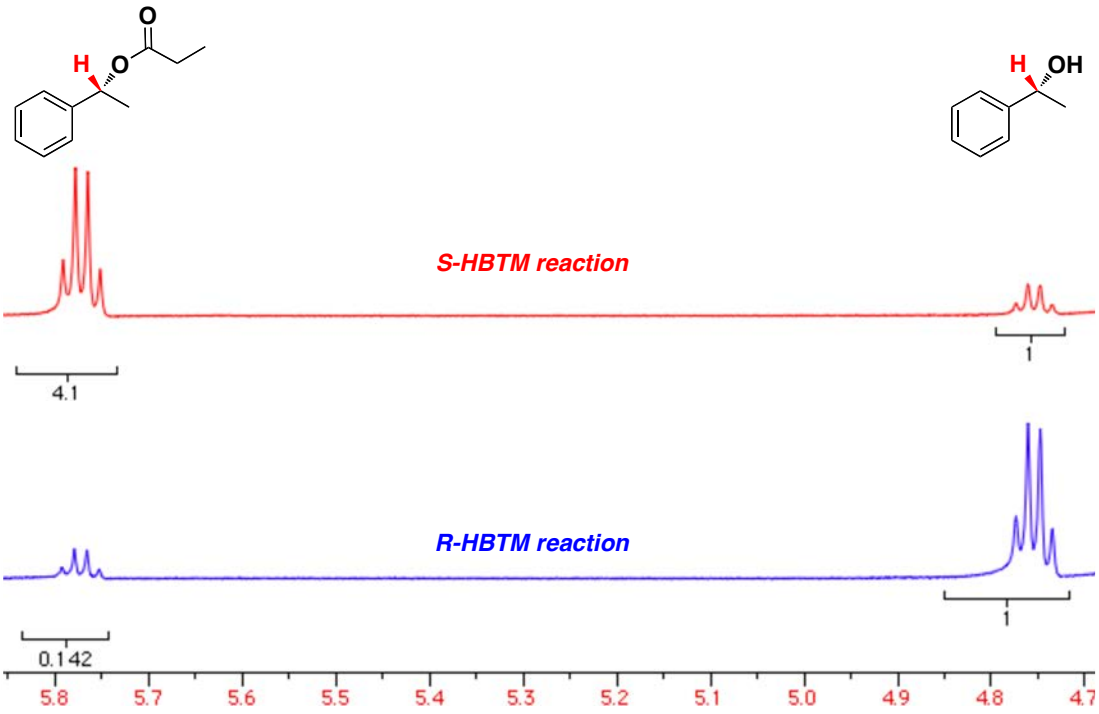
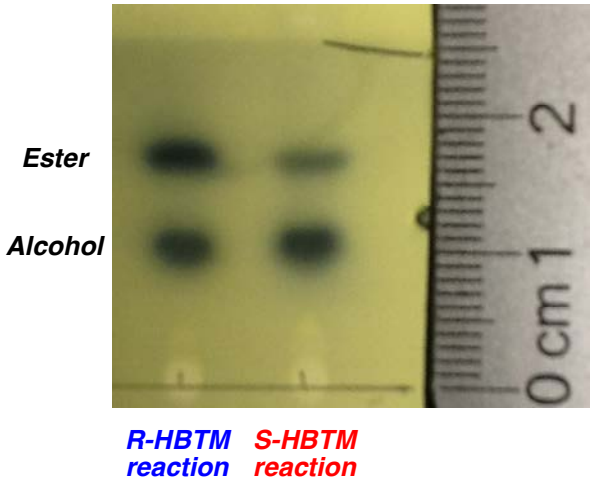


(b)

Entry 2. (a) TLC of parallel reactions (b) ^{1}H NMR Spectra of parallel reactions in $CDCl_3$ at 500 MHz.



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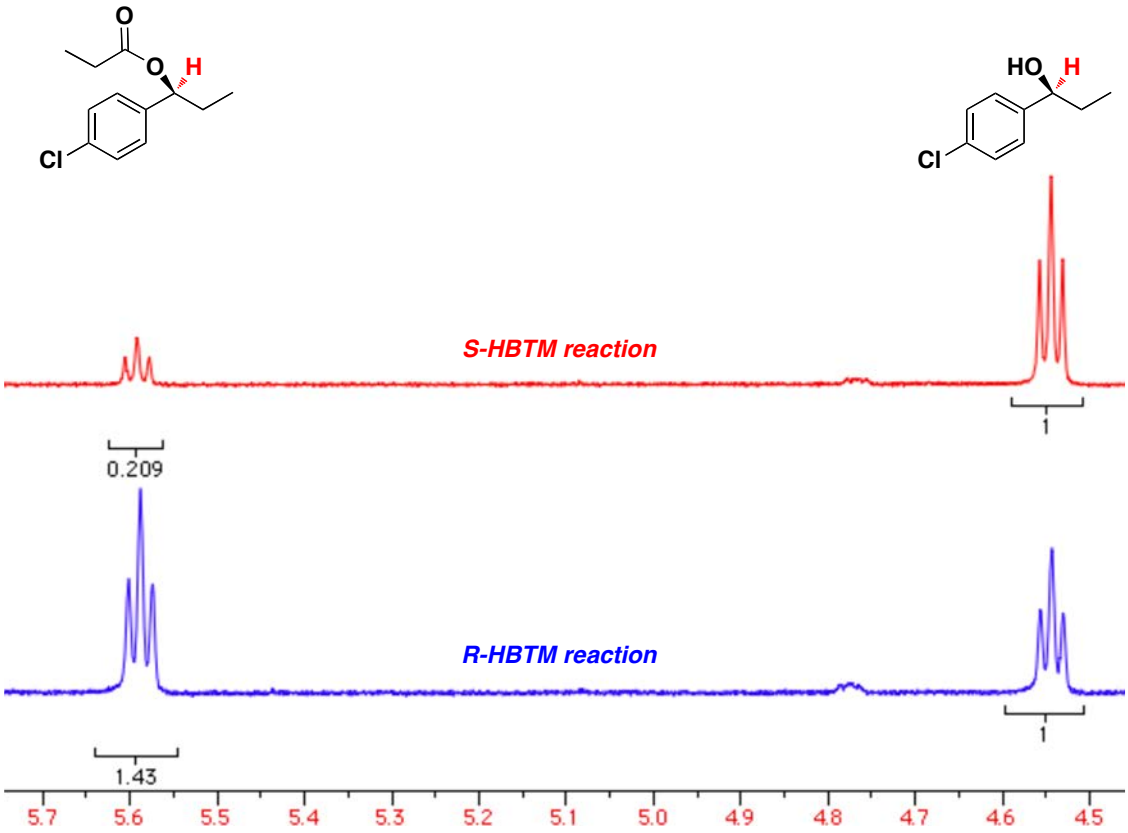

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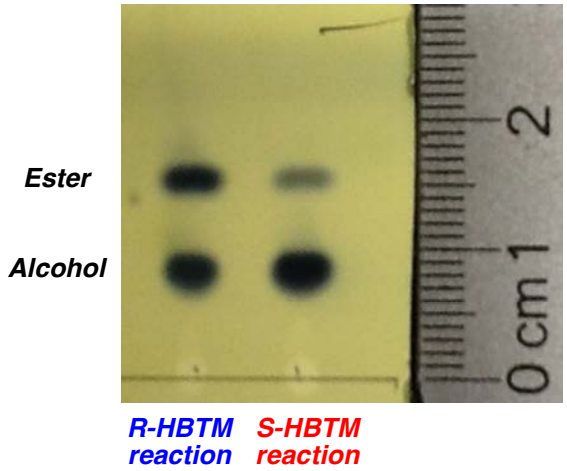
Entry 3. (a) TLC of parallel reactions (b) ^{1}H NMR Spectra of parallel reactions in $CDCl_3$ at 500 MHz.



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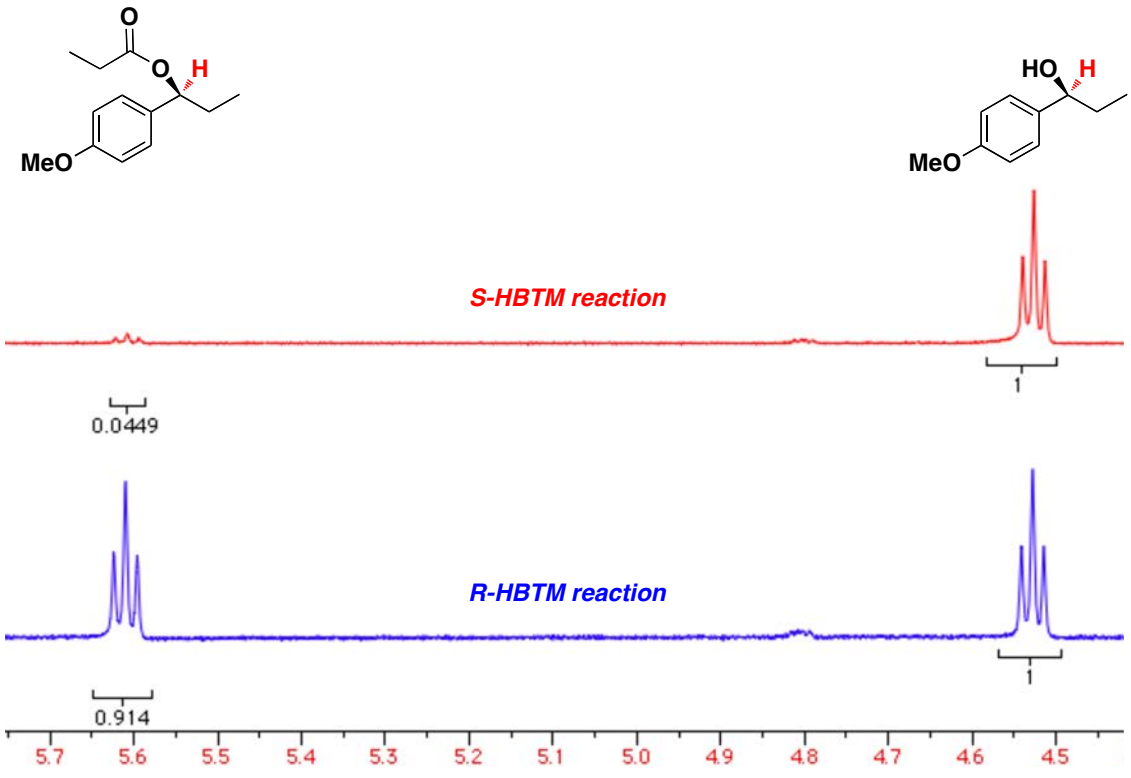

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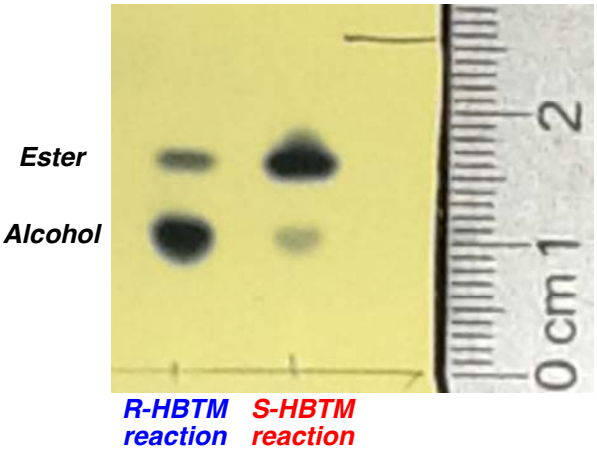
Entry 4. (a) TLC of parallel reactions (b) ^{1}H NMR Spectra of parallel reactions in $CDCl_3$ at 500 MHz.



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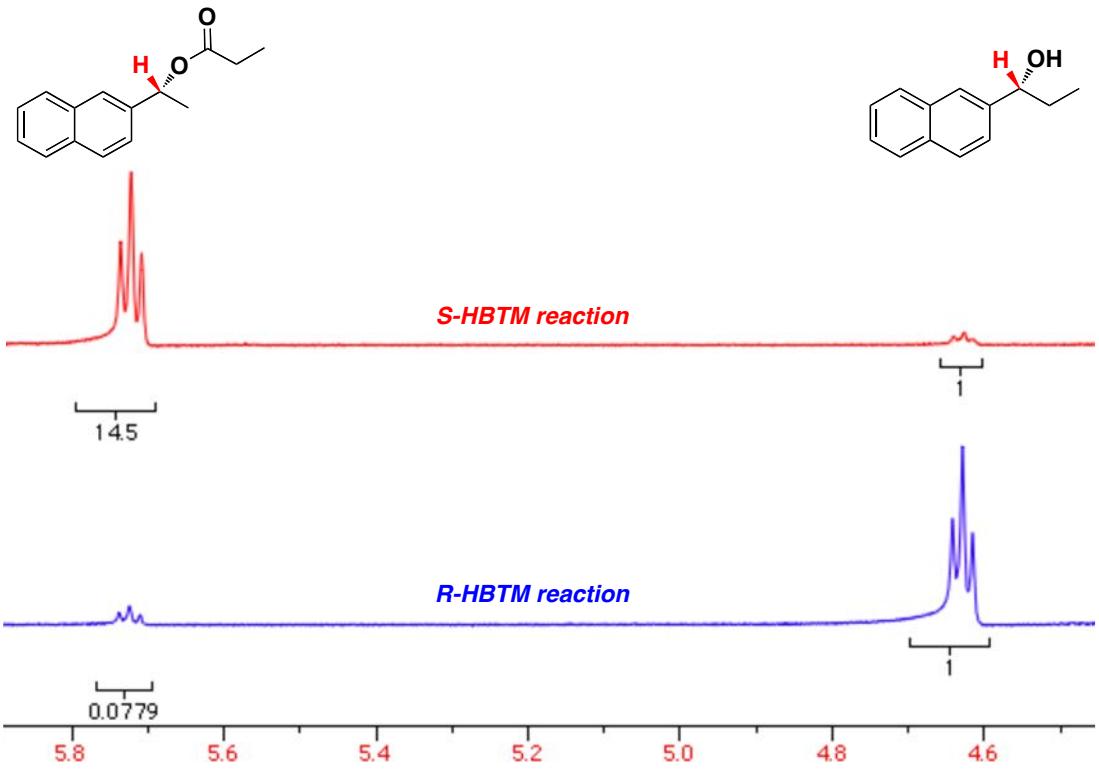
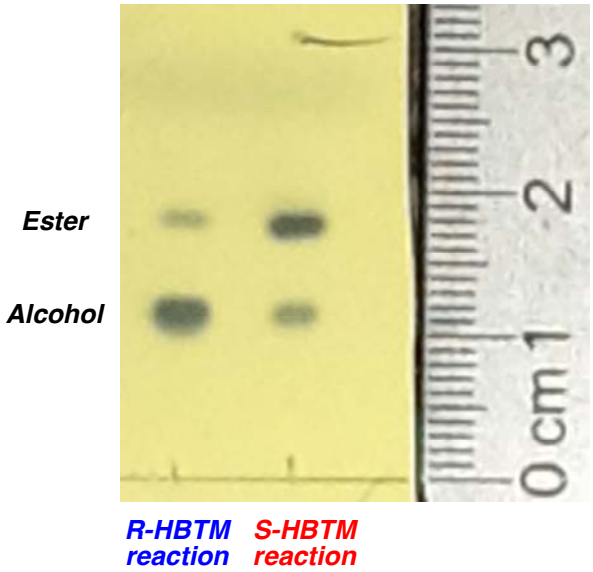


(b)

Entry 5. (a) TLC of parallel reactions (b) ^{1}H NMR Spectra of parallel reactions in $CDCl_3$ at 500 MHz.



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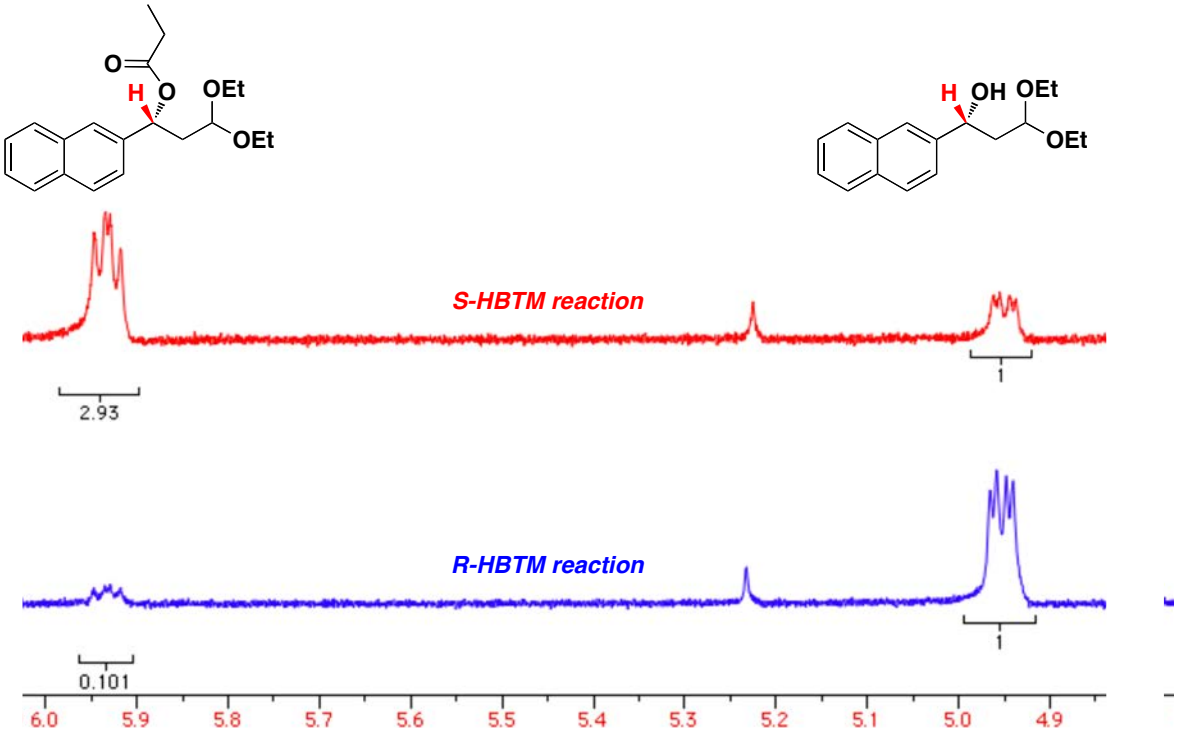
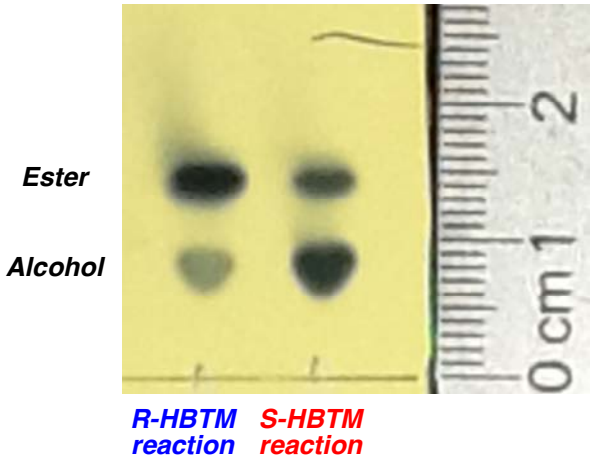


(b)

Entry 6. (a) TLC of parallel reactions (b) ^{1}H NMR Spectra of parallel reactions in $CDCl_3$ at 500 MHz.



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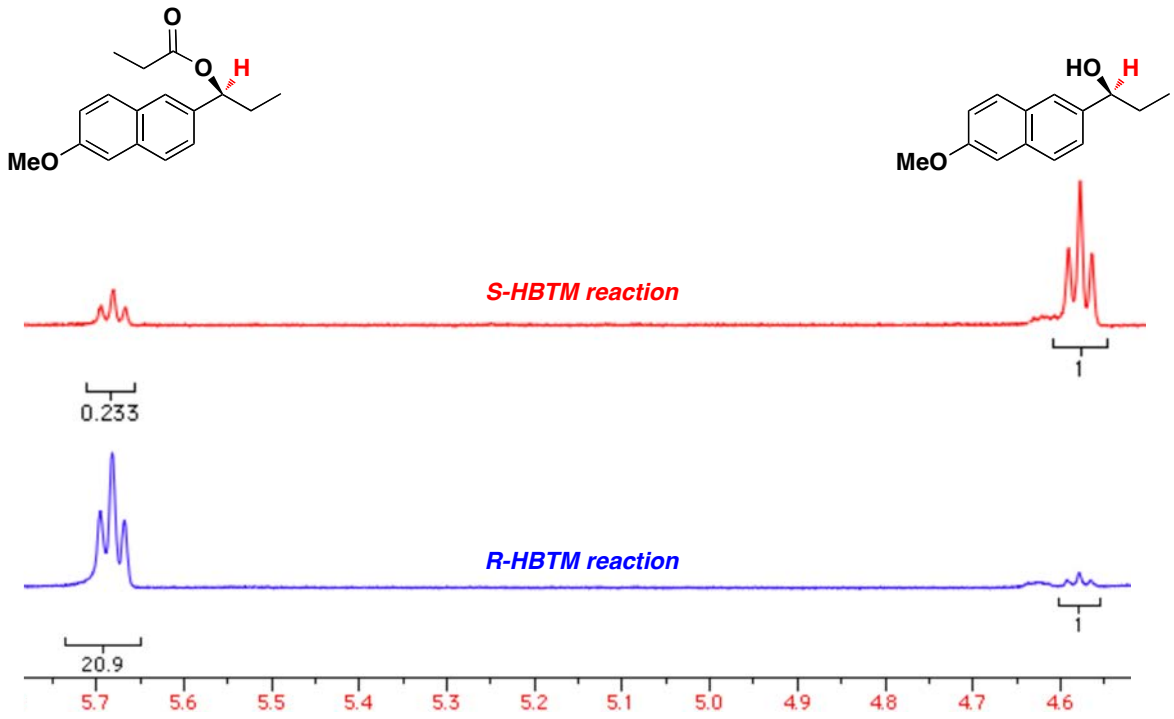
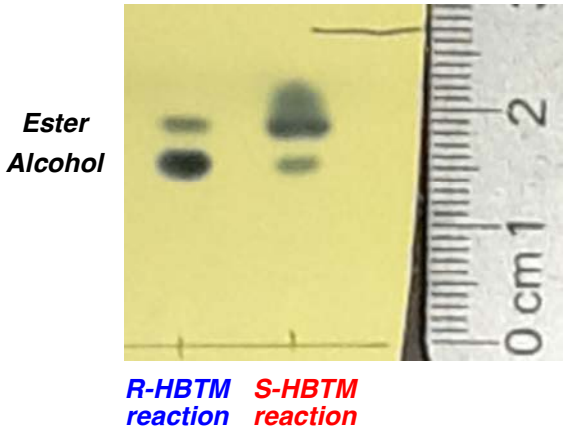


(b)

Entry 7. (a) TLC of parallel reactions (b) ^{1}H NMR Spectra of parallel reactions in $CDCl_3$ at 500 MHz.



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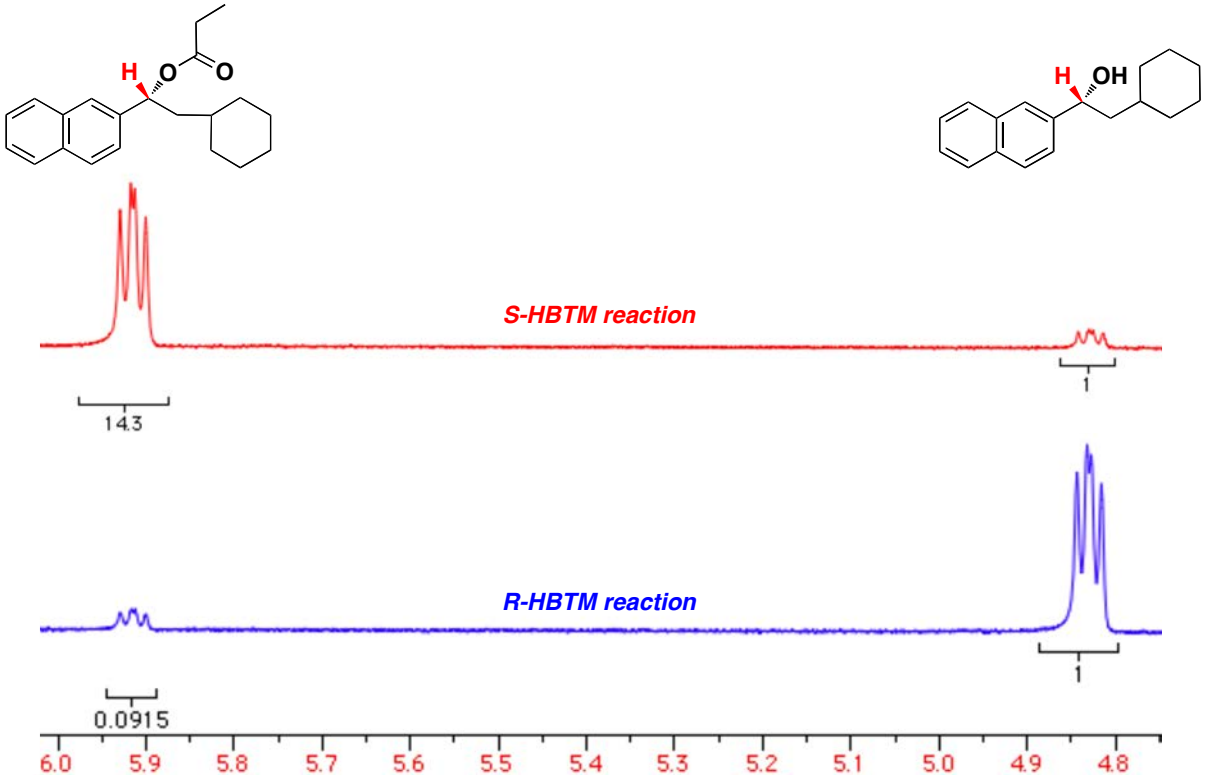
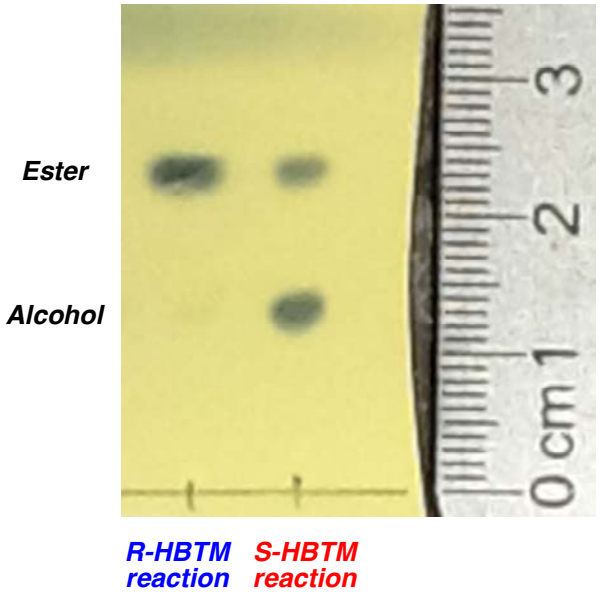


(b)

Entry 8. (a) TLC of parallel reactions (b) ^{1}H NMR Spectra of parallel reactions in $CDCl_3$ at 500 MHz.



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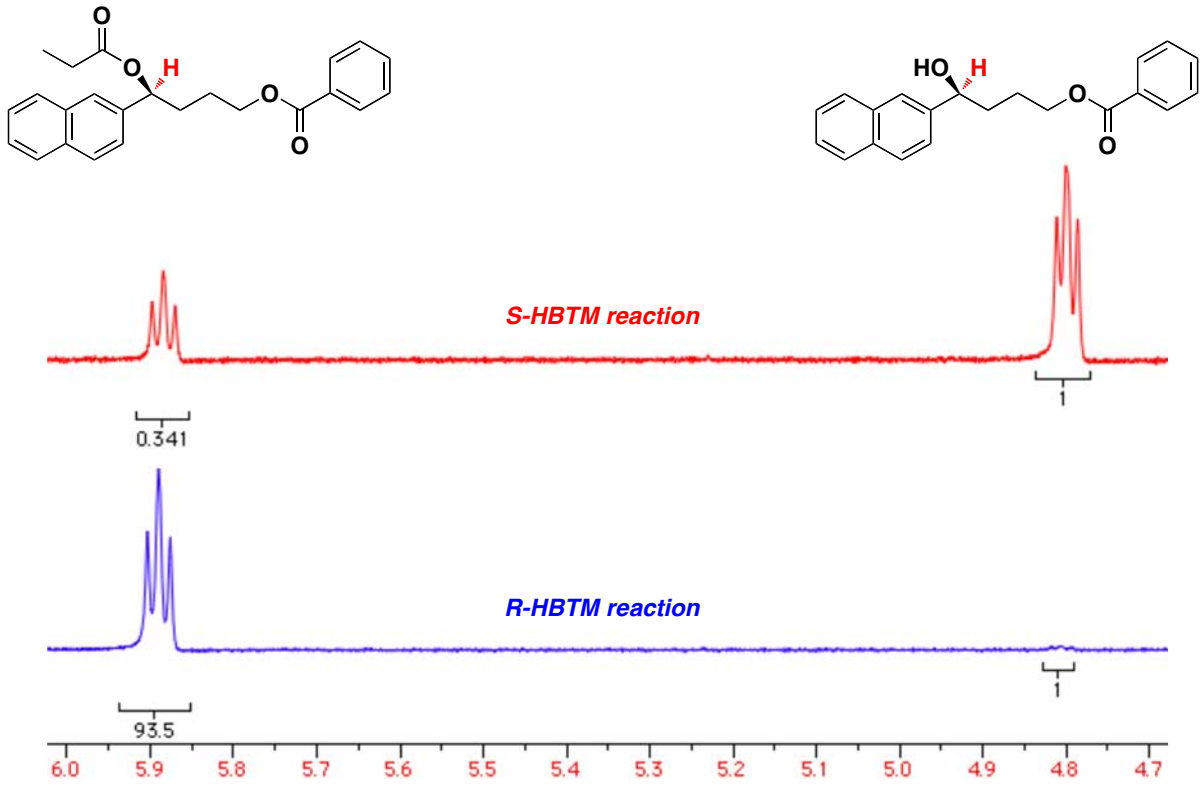

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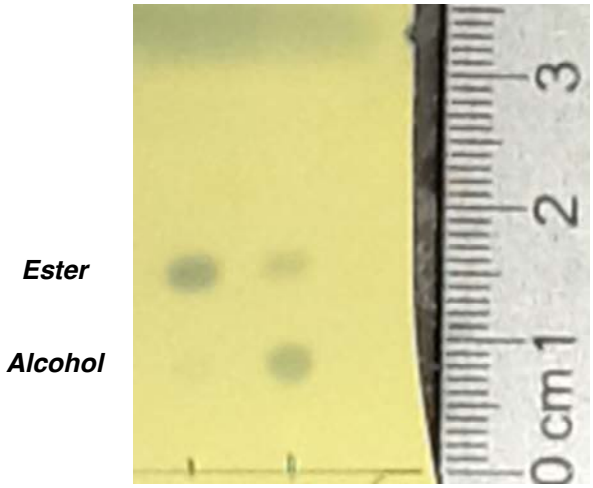
Entry 9. (a) TLC of parallel reactions (b) ^{1}H NMR Spectra of parallel reactions in $CDCl_3$ at 500 MHz.



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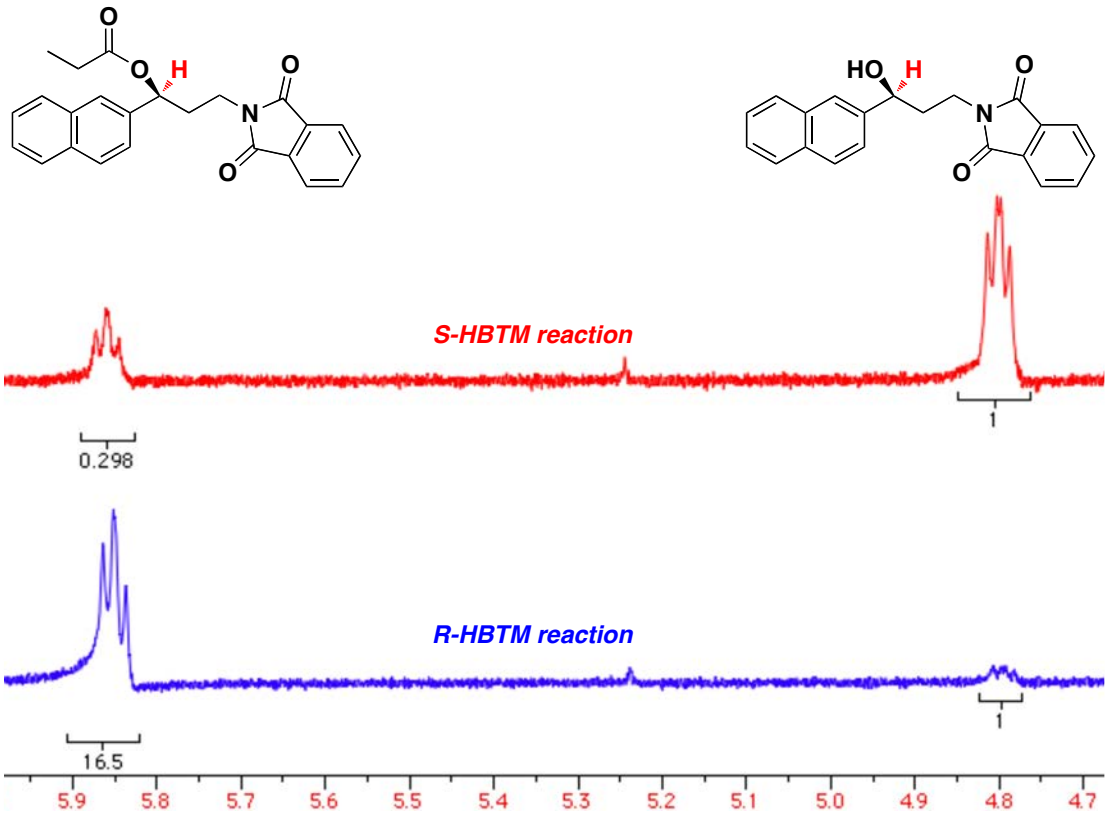

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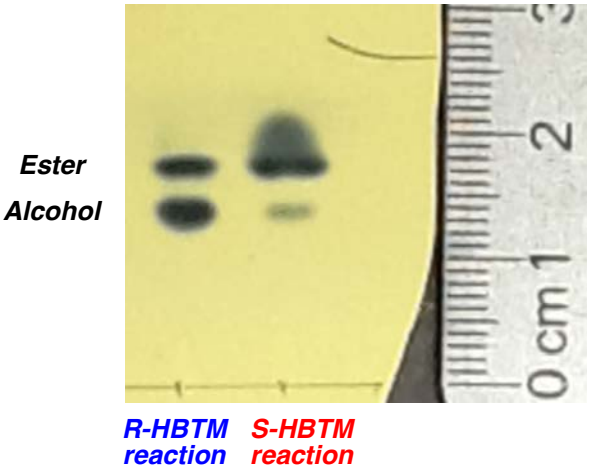
Entry 10. (a) TLC of parallel reactions (b) ^{1}H NMR Spectra of parallel reactions in $CDCl_3$ at 500 MHz.



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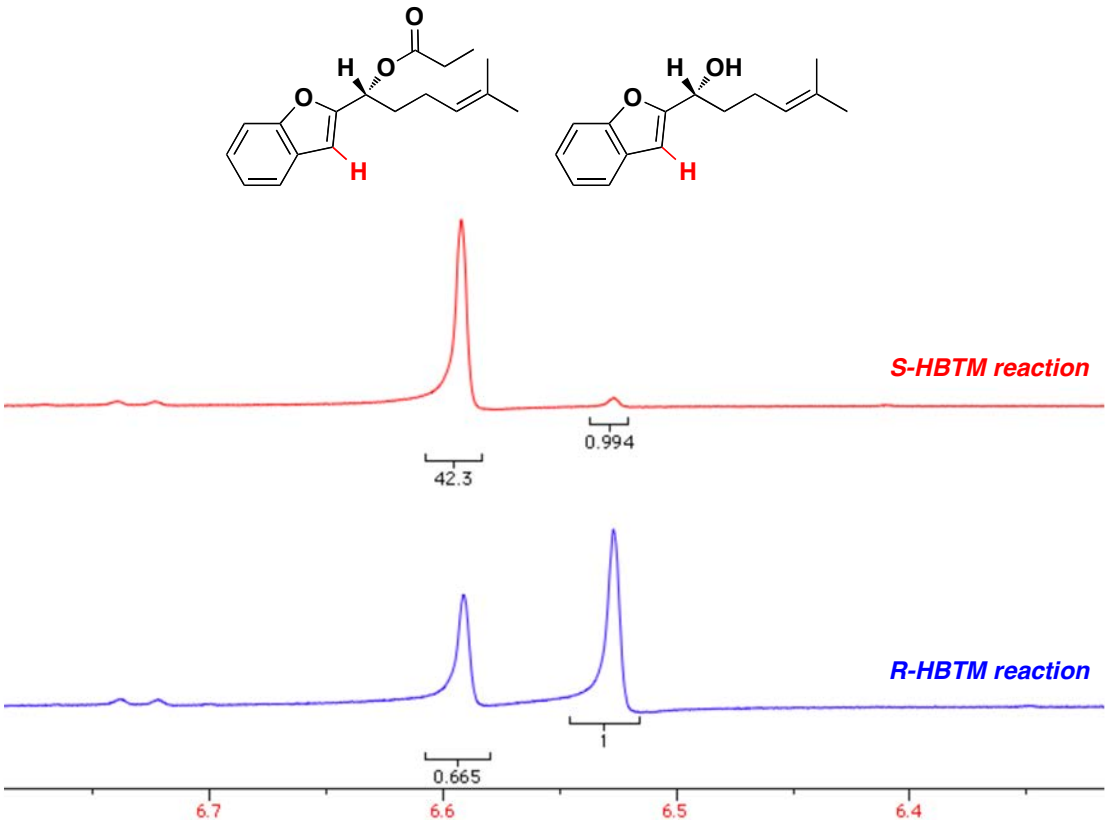
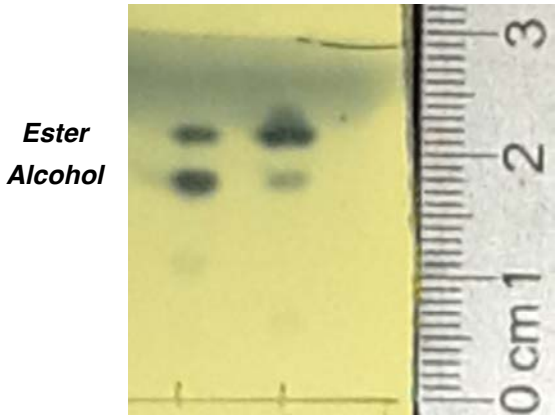


(b)

Entry 11. (a) TLC of parallel reactions (b) ^{1}H NMR Spectra of parallel reactions in $CDCl_3$ at 500 MHz.



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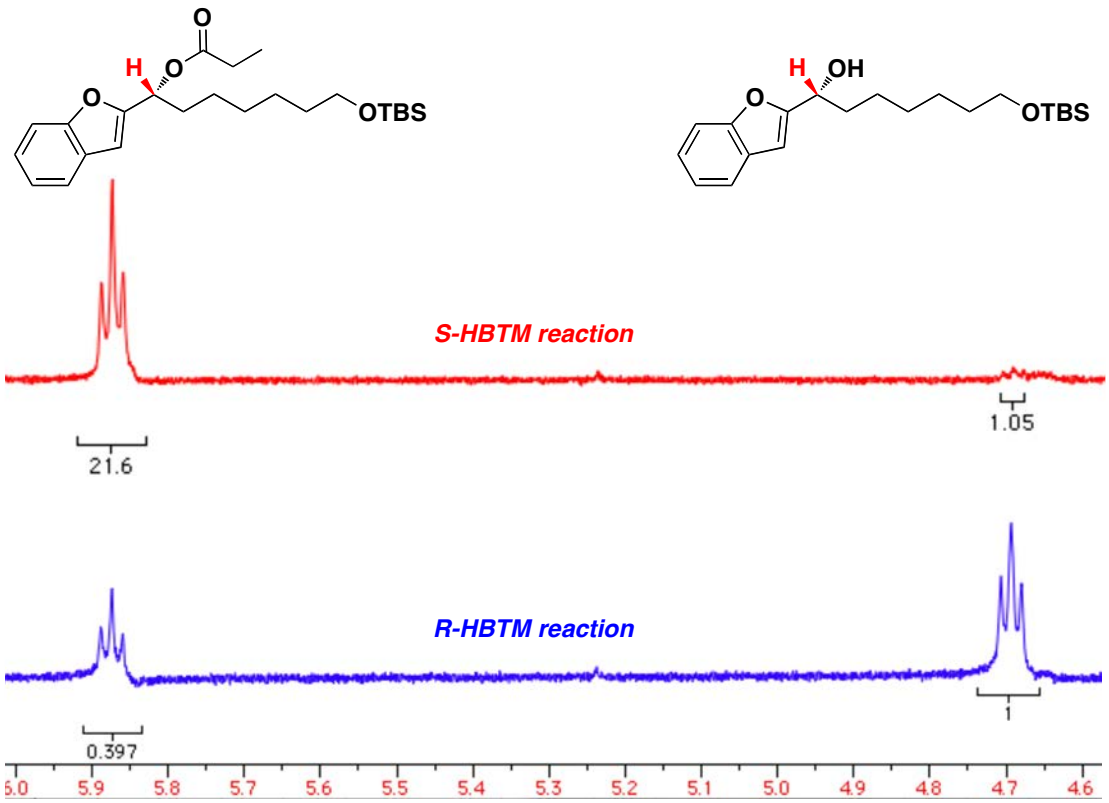
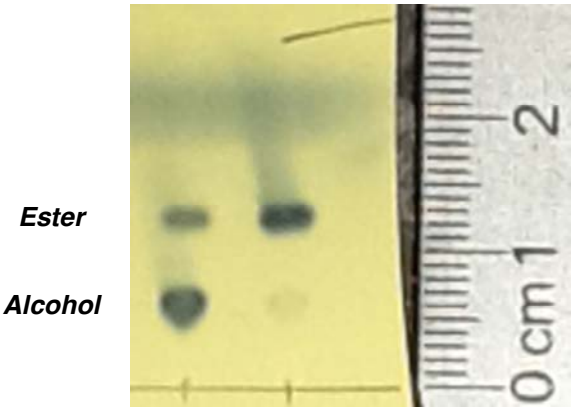
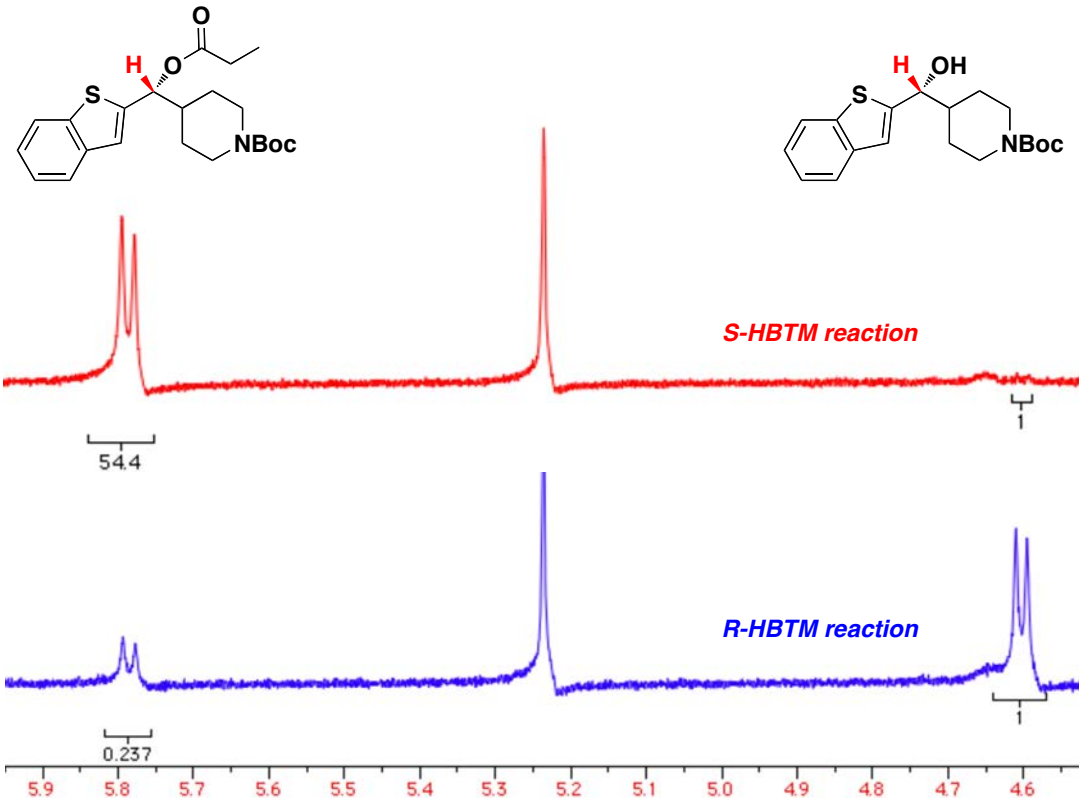


(b)

Entry 12. (a) TLC of parallel reactions (b) ^{1}H NMR Spectra of parallel reactions in $CDCl_3$ at 500 MHz.

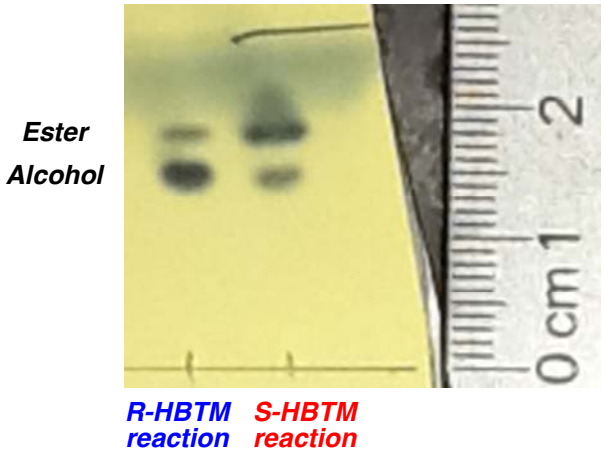


(a)



(b)

Entry 13. (a) TLC of parallel reactions (b) ^{1}H NMR Spectra of parallel reactions in $CDCl_3$ at 500 MHz.



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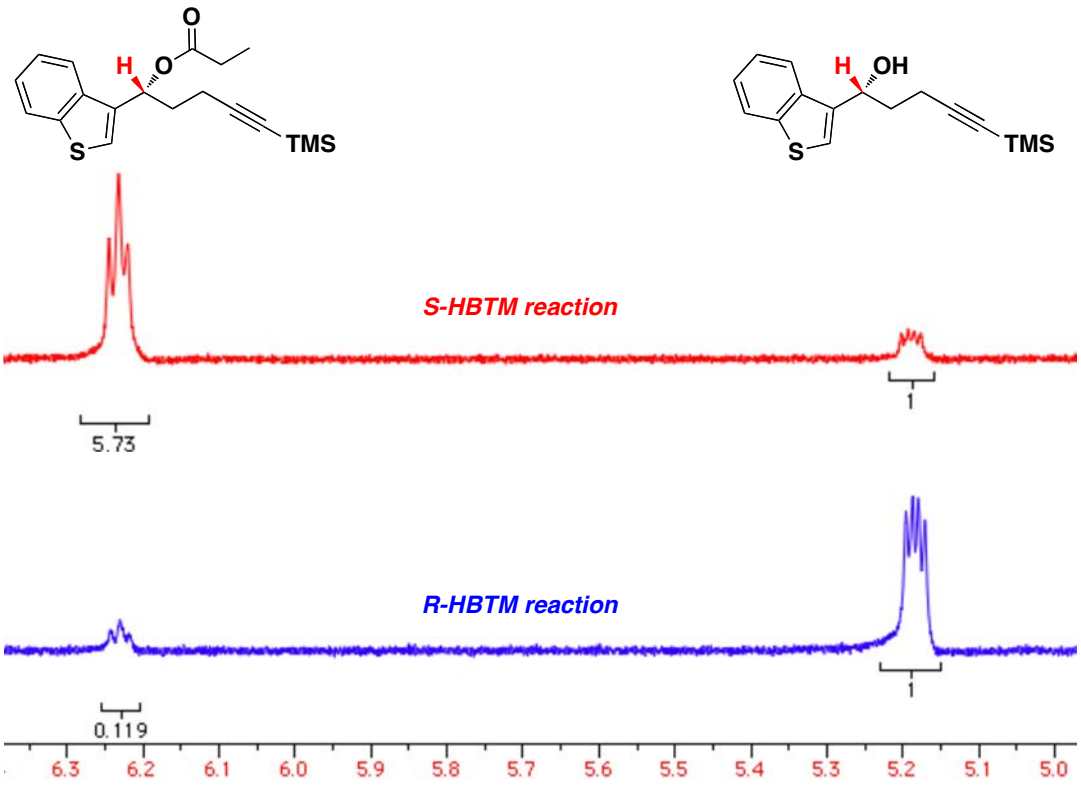
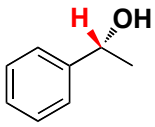


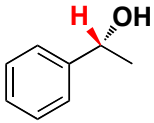
(b)

^{1}H NMR in $CDCl_3$ at 500 MHz



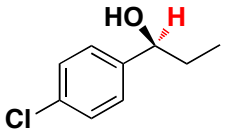
Entry 1 with R-HBTM

^{1}H NMR in $CDCl_3$ at 500 MHz



Entry 1 with S-HBTM

^{1}H NMR in $CDCl_3$ at 500 MHz



Entry 2 with R-HBTM

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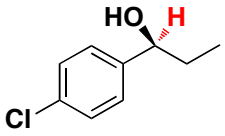
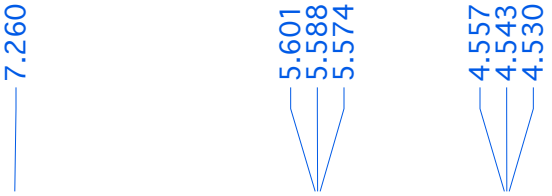
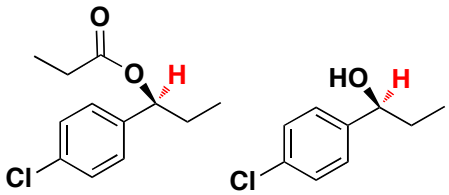


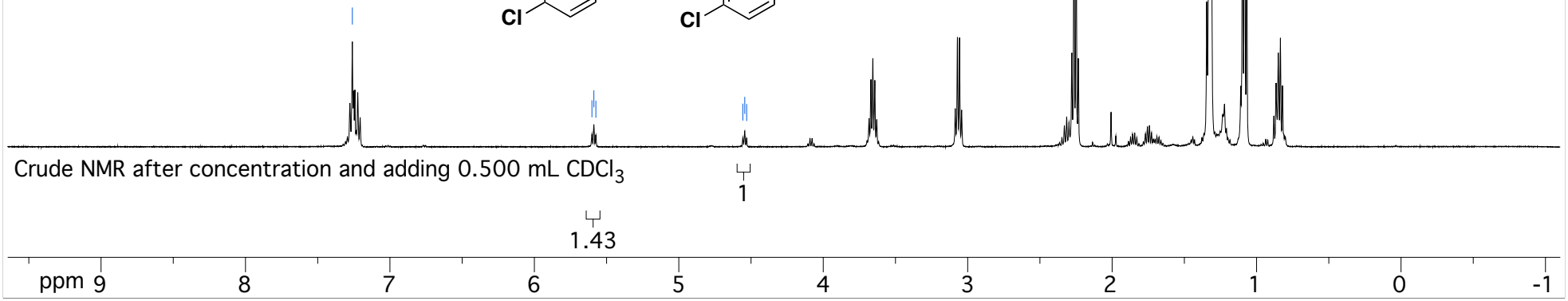
Entry 2 with R-HBTM



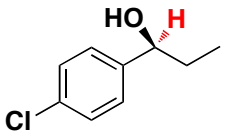
Crude NMR before concentration to remove methanol



Crude NMR after concentration and adding 0.500 mL $CDCl_3$

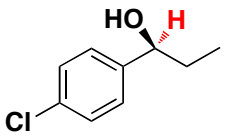


^{1}H NMR in $CDCl_3$ at 500 MHz



Entry 2 with S-HBTM

^{1}H NMR in $CDCl_3$ at 500 MHz



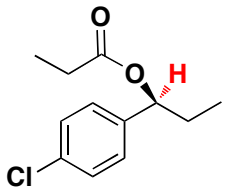
Entry 2 with S-HBTM

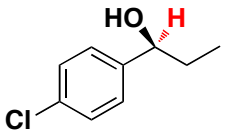
7.260

5.602
5.588
5.573

4.556
4.543
4.529

Crude NMR before concentration to remove methanol





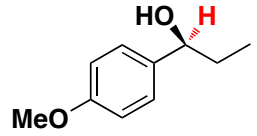
Crude NMR after concentration and adding 0.500 mL $CDCl_3$

1

0.209

ppm 9 8 7 6 5 4 3 2 1 0 -1

^{1}H NMR in $CDCl_3$ at 500 MHz



Entry 3 with R-HBTM

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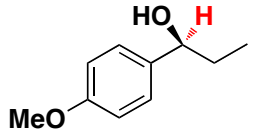
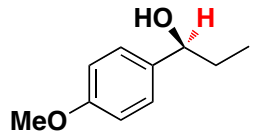


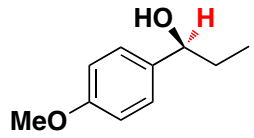
Entry 3 with R-HBTM

^{1}H NMR in $CDCl_3$ at 500 MHz



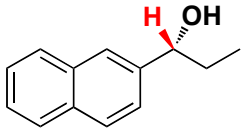
Entry 3 with S-HBTM

^{1}H NMR in $CDCl_3$ at 500 MHz



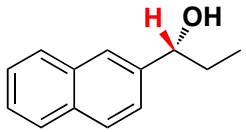
Entry 3 with S-HBTM

^{1}H NMR in $CDCl_3$ at 500 MHz



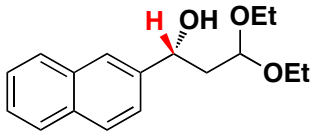
Entry 4 with R-HBTM

^{1}H NMR in $CDCl_3$ at 500 MHz



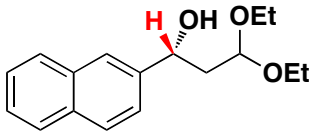
Entry 4 with S-HBTM

^{1}H NMR in $CDCl_3$ at 500 MHz



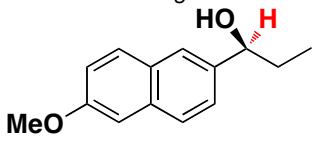
Entry 5 with R-HBTM

^{1}H NMR in $CDCl_3$ at 500 MHz



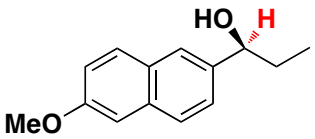
Entry 5 with S-HBTM

^{1}H NMR in $CDCl_3$ at 500 MHz

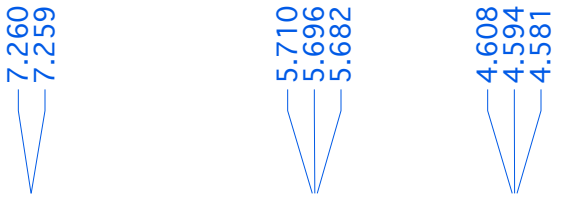


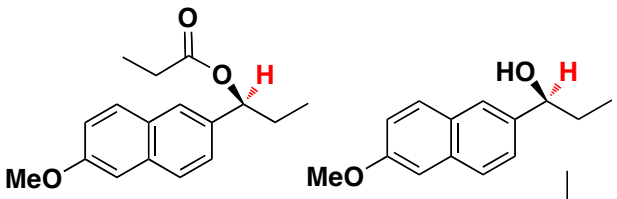
Entry 6 with R-HBTM

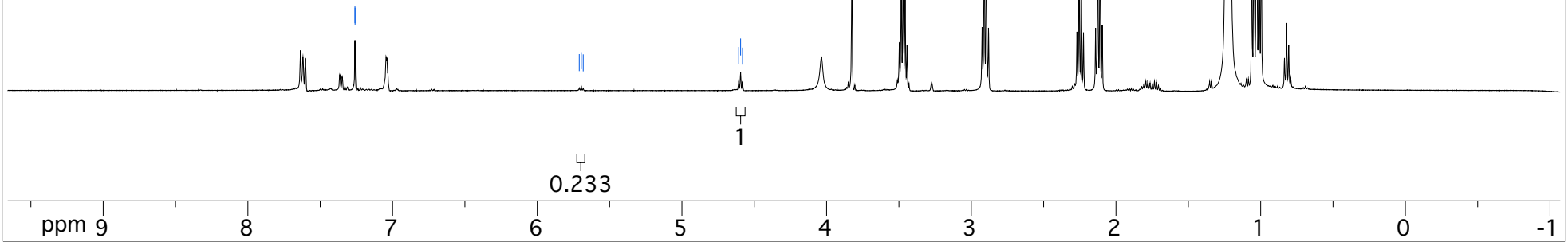
^{1}H NMR in $CDCl_3$ at 500 MHz



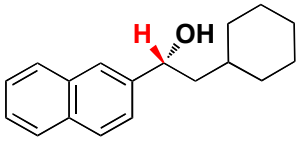
Entry 6 with S-HBTM





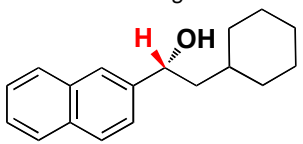


^{1}H NMR in $CDCl_3$ at 500 MHz

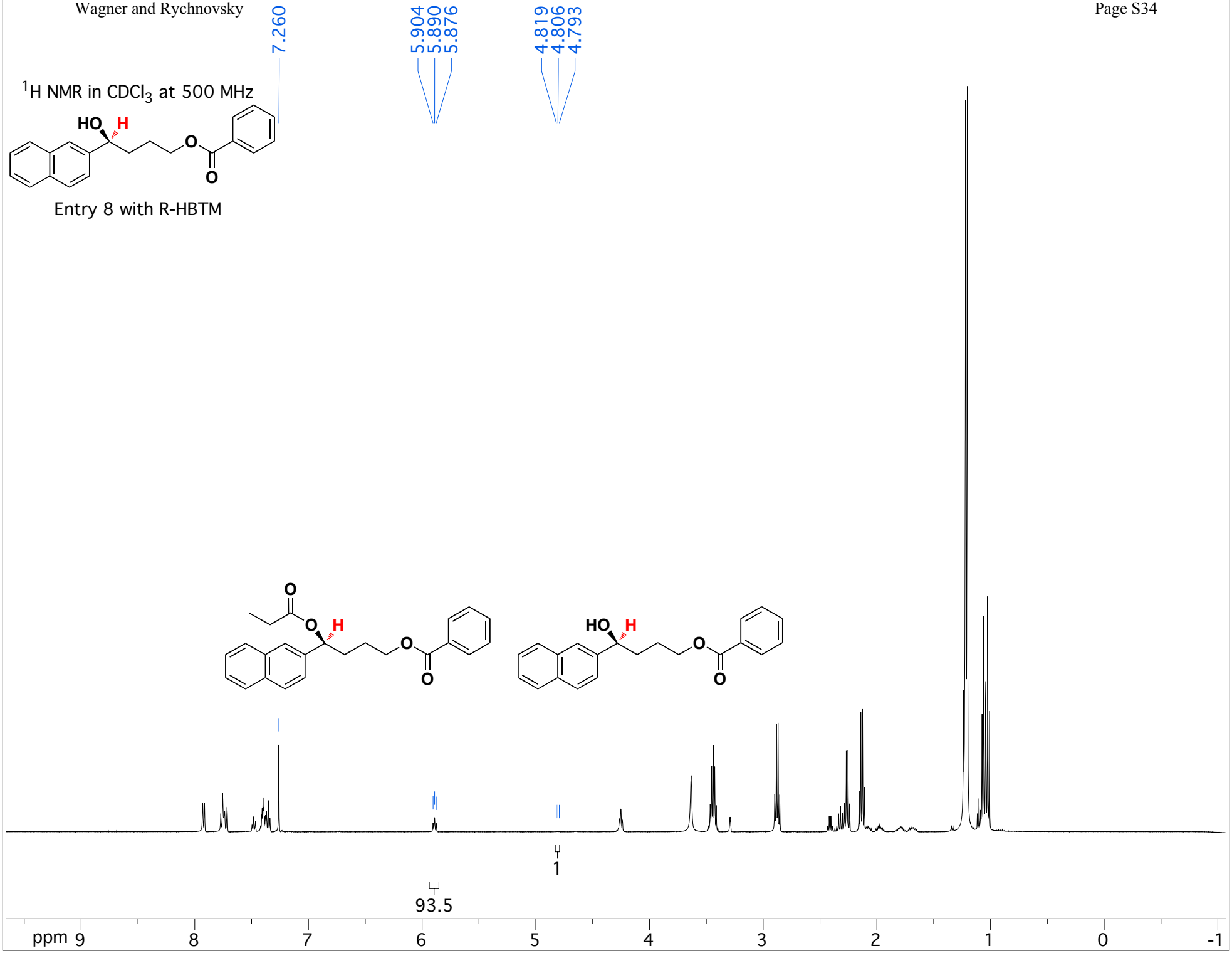


Entry 7 with R-HBTM

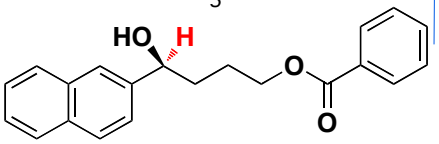
^{1}H NMR in $CDCl_3$ at 500 MHz



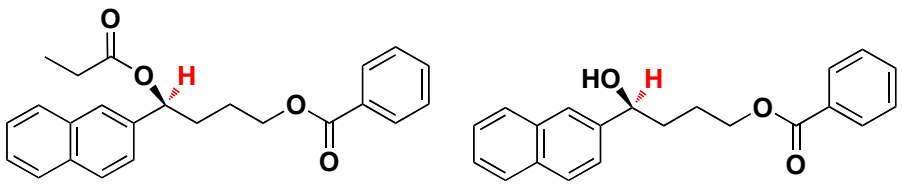
Entry 7 with S-HBTM


7.260
5.904
5.890
5.876
4.819
4.806
4.793
^{1}H NMR in $CDCl_3$ at 500 MHz
HO
H
O
O
Entry 8 with R-HBTM
O
O
H
O
O
HO
H
O
O
1
93.5
ppm 9
8
7
6
5
4
3
2
1
0
-1

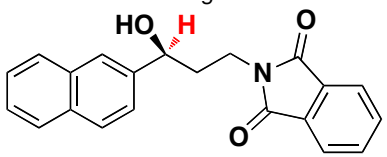
^{1}H NMR in $CDCl_3$ at 500 MHz



Entry 8 with S-HBTM

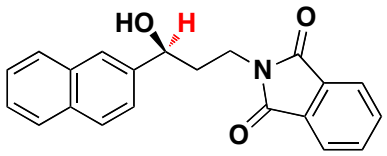


^{1}H NMR in $CDCl_3$ at 500 MHz



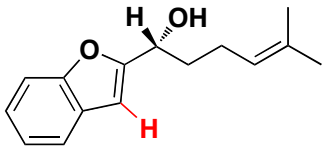
Entry 9 with R-HBTM

^{1}H NMR in $CDCl_3$ at 500 MHz

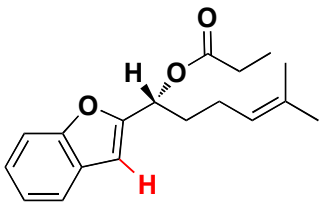


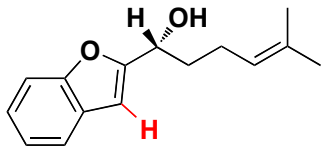
Entry 9 with S-HBTM

^{1}H NMR in $CDCl_3$ at 500 MHz

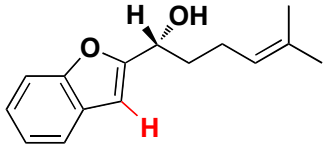


Entry 10 with R-HBTM



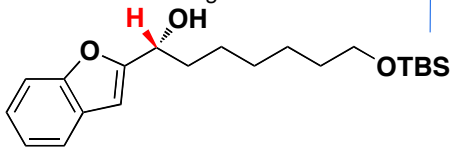


^{1}H NMR in $CDCl_3$ at 500 MHz



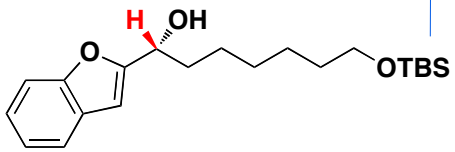
Entry 10 with S-HBTM

^{1}H NMR in $CDCl_3$ at 500 MHz



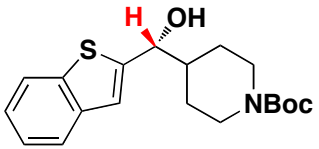
Entry 11 with R-HBTM

^{1}H NMR in $CDCl_3$ at 500 MHz



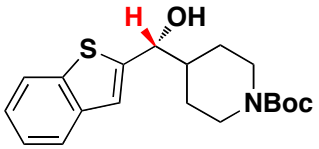
Entry 11 with S-HBTM

^{1}H NMR in $CDCl_3$ at 500 MHz



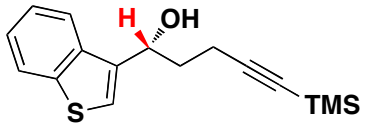
Entry 12 with R-HBTM

^{1}H NMR in $CDCl_3$ at 500 MHz



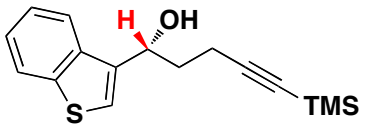
Entry 12 with S-HBTM

^{1}H NMR in $CDCl_3$ at 500 MHz



Entry 13 with R-HBTM

^{1}H NMR in $CDCl_3$ at 500 MHz



Entry 13 with S-HBTM

Chiral Analytical Traces for Entries 1-3, 6-7.

HPLC determinations of enantiopurity were performed on an Agilent 1100 Series instrument using isopropyl alcohol (OmniSolv®) and n-hexane (HPLC grade, 95% min) with Daicel™ columns.

Entry 1 (S47-S48):

HPLC analysis (Chiralcel® OD with OD guard, 5.0% *i*PrOH/n-Hexane, 1.0 mL/min) indicated >99:<1 er; t_R (major) = 9.6 minutes, t_R (minor) = 12.4 minutes.

Entry 2 (S49-S50):

HPLC analysis (Chiralpak® OB-H with OB guard, 5.0% *i*PrOH/n-Hexane, 0.80 mL/min) indicated 85:15 er; t_R (major) = 9.6 minutes, t_R (minor) = 11.1 minutes.

Entry 3 (S51-S52):

HPLC analysis (Chiralpak® AD with AD guard, 5.0% *i*PrOH/n-Hexane, 1.0 mL/min) indicated 98:2 er; t_R (major) = 12.0 minutes, t_R (major) = 13.5 minutes.

SFC determinations of enantiopurity were performed on a Berger Analytical instrument using a Daicel™ column (100 bar, 50 °C, 215 nm).

Entry 6 (S53-S54):

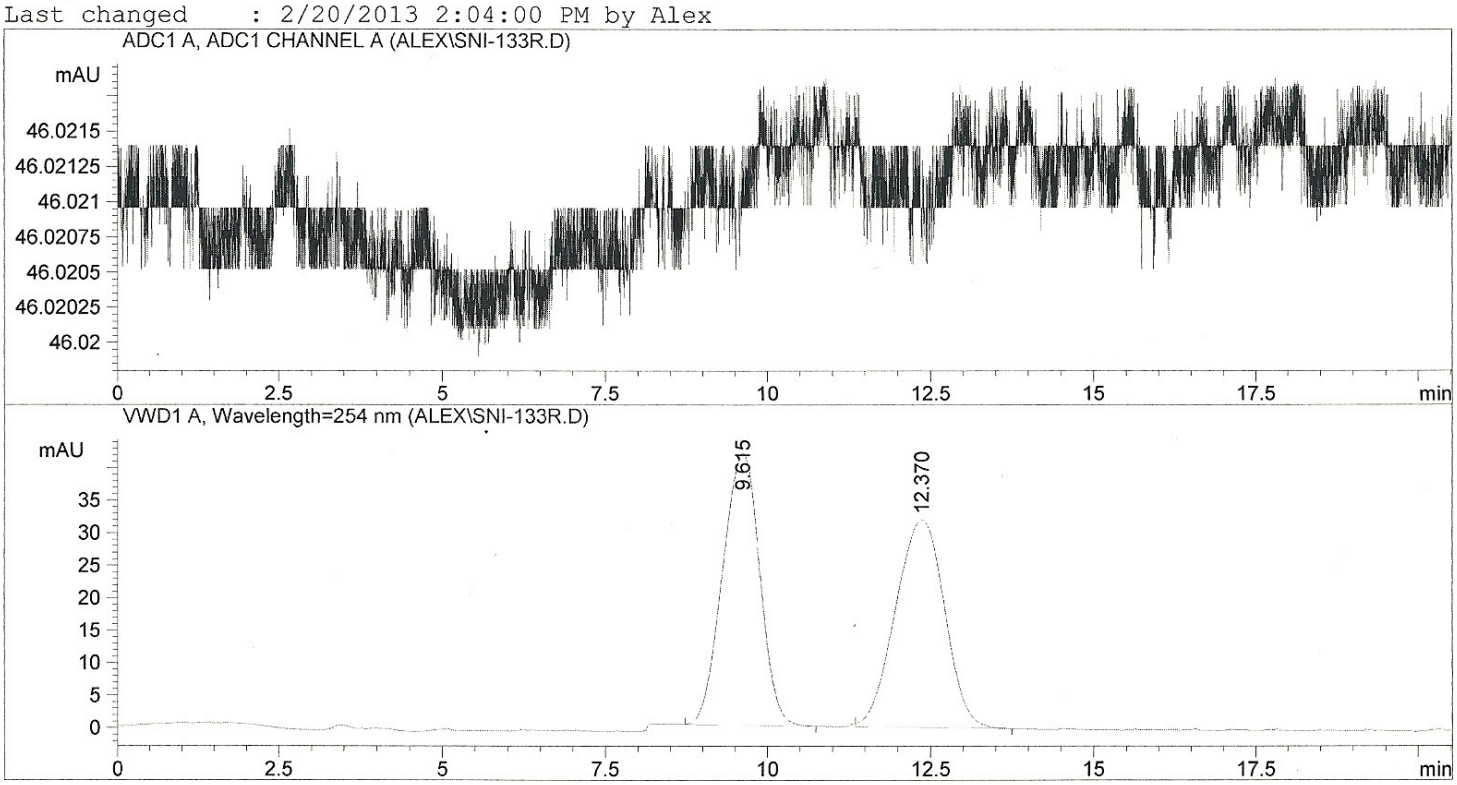
SFC analysis (Chiralpak® OD-H, 12.5% *i*PrOH, 3.0 mL/min) indicated 97:3 er; t_R (major) = 5.3 minutes, t_R (minor) = 6.5 minutes.

Entry 7 (S55-S56):

SFC analysis (Chiralpak® AS-H, 3.0% *i*PrOH, 3.0 mL/min) indicated 98:2 er; t_R (minor) = 12.2 minutes, t_R (major) = 12.8 minutes.

Column OD with guard 5% iPrOH/Hexanes 1.00 mL 38 bar

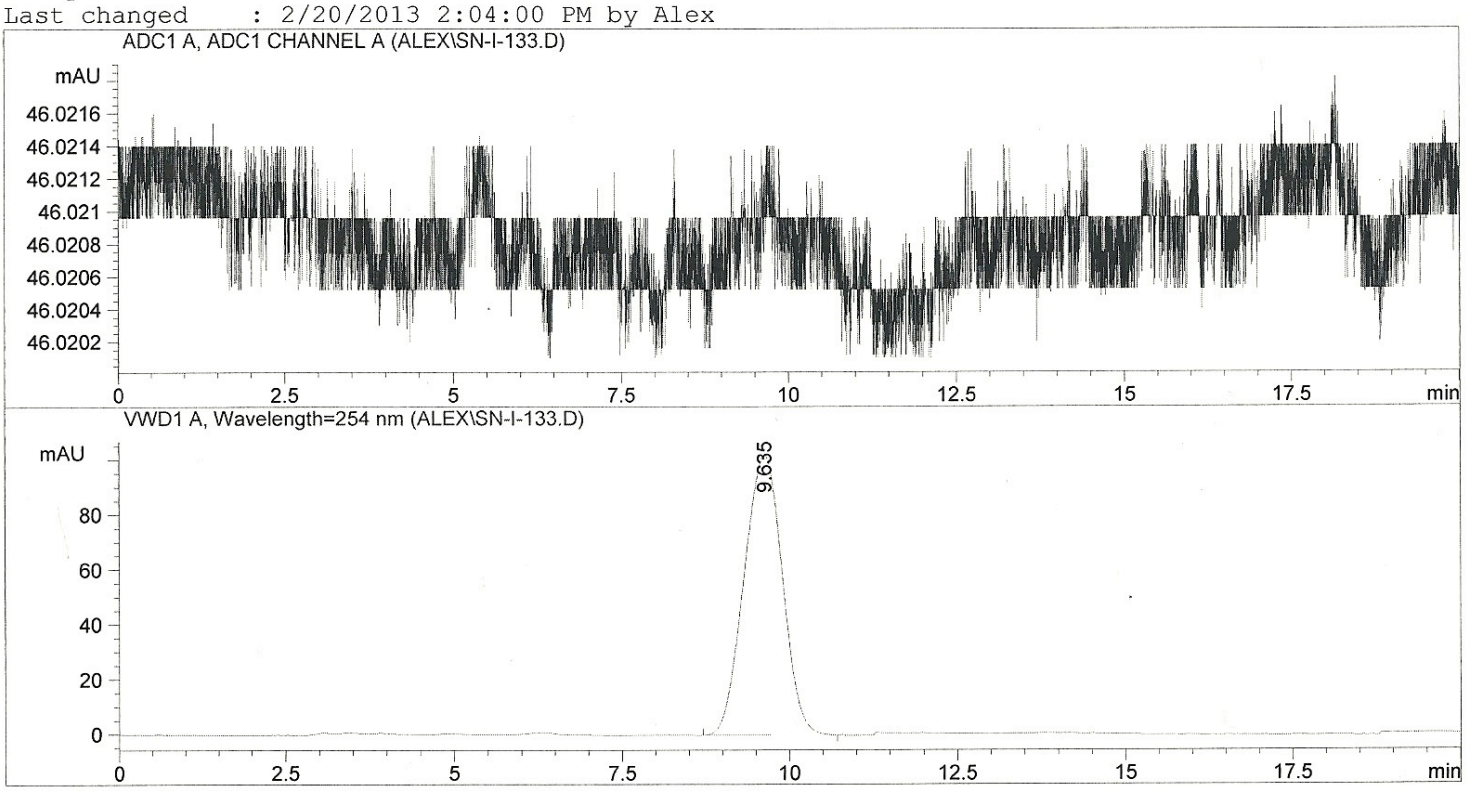
```
==========================================================================
Injection Date  : 9/28/2012 4:44:16 PM
Sample Name     : SN-1-133-RacOH                  Location : Vial 42
Acq. Operator   : Alex
                                                  Inj Volume : 10 µl
Acq. Method     : C:\HPCHEM\1\METHODS\ALEX.M
Last changed    : 9/28/2012 4:44:17 PM by Alex
                  (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\ALEX.M
Last changed    : 2/20/2013 2:04:00 PM by Alex
```




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

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :     10.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: ADC1 A, ADC1 CHANNEL A


Signal 2: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   9.615 BB    0.6355 1675.50940   41.89484  50.0590
   2  12.370 VB    0.7585 1671.56042   31.97147  49.9410

Totals :                  3347.06982   73.86631

 Results obtained with enhanced integrator!
==========================================================================
                          *** End of Report ***
```

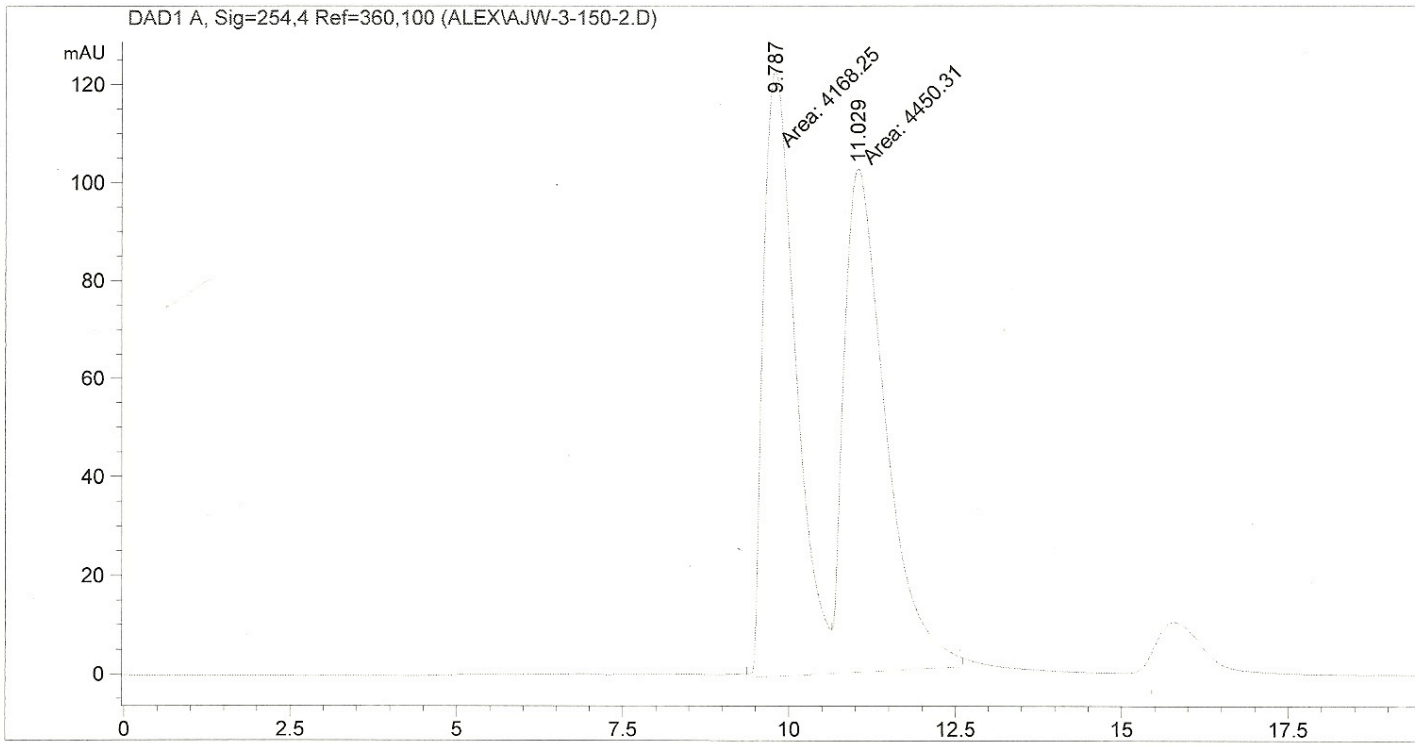
Column OD with guard 5% iPrOH/Hexanes 1.00 mL 38 bar

```
==========================================================================
Injection Date  : 9/28/2012 4:22:04 PM
Sample Name     : SN-1-133-OH                    Location : Vial 41
Acq. Operator   : Alex
                                                 Inj Volume : 10 µl
Acq. Method     : C:\HPCHEM\1\METHODS\ALEX.M
Last changed    : 9/28/2012 3:34:42 PM by Alex
                  (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\ALEX.M
Last changed    : 2/20/2013 2:04:00 PM by Alex
```



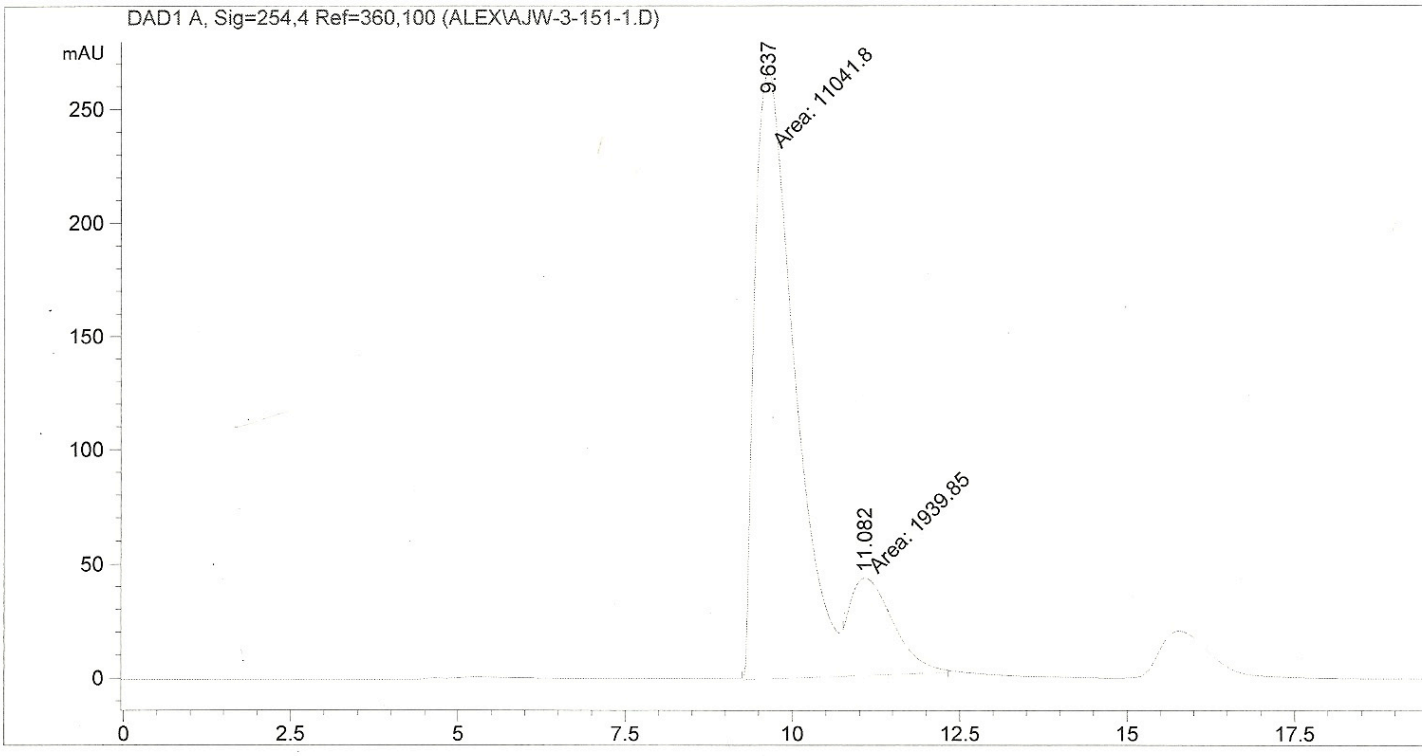

```
==========================================================================
                          Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :     10.00000  [ng/ul]    (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: ADC1 A, ADC1 CHANNEL A


Signal 2: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   9.635 BB    0.6300 4094.94434  102.00067 100.0000

Totals :                  4094.94434  102.00067

 Results obtained with enhanced integrator!
==========================================================================
                          *** End of Report ***
```

```
==========================================================================
Acq. Operator    : Alex
Acq. Instrument  : Instrument 2                    Location : Vial 61
Injection Date   : 2/25/2013 2:32:16 PM
                                                   Inj Volume : 30 µl
Acq. Method      : C:\CHEM32\2\METHODS\JONLAM.M
Last changed     : 2/25/2013 2:30:49 PM by Alex
                   (modified after loading)
Analysis Method  : C:\CHEM32\2\DATA\JONLAM\JKL-04-154.D\DA.M (JONLAM.M)
Last changed     : 2/25/2013 1:10:16 PM by Jon Lam
Sample Info      : Chiralpak OB-H + OB Guard, 5% IPA/Hexanes, 0.8 ml/min,
                   42 bar
```




```
==========================================================================
                          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 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   9.787 MF    0.5648 4168.24658  123.00746  48.3636
   2  11.029 FM    0.7247 4450.30811  102.34229  51.6364

Totals :                  8618.55469  225.34975
```

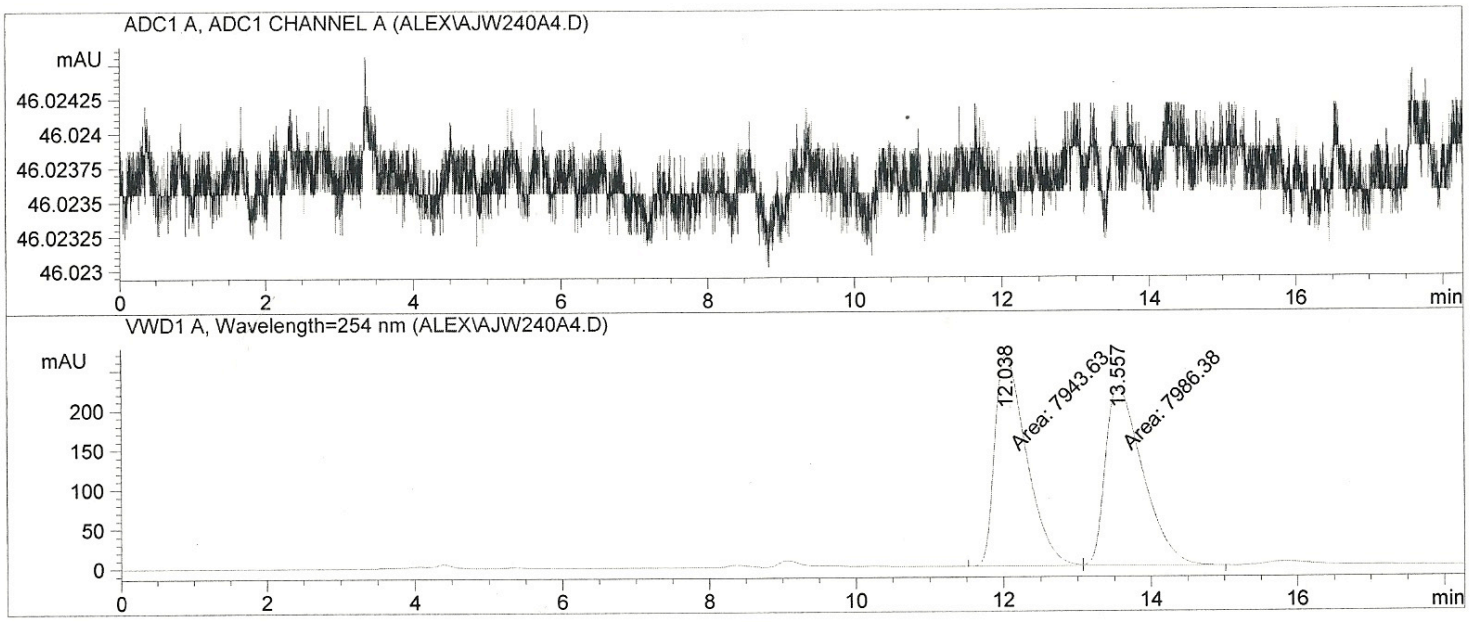
```
==========================================================================
Acq. Operator   : Alex
Acq. Instrument : Instrument 2                    Location : Vial 62
Injection Date  : 2/25/2013 2:54:32 PM
                                                  Inj Volume : 30 µl
Acq. Method     : C:\CHEM32\2\METHODS\JONLAM.M
Last changed    : 2/25/2013 2:52:37 PM by Alex
                  (modified after loading)
Analysis Method : C:\CHEM32\2\DATA\JONLAM\JKL-04-154.D\DA.M (JONLAM.M)
Last changed    : 2/25/2013 1:10:16 PM by Jon Lam
Sample Info     : Chiralpak OB-H + OB Guard, 5% IPA/Hexanes, 0.8 ml/min,
                  42 bar
```




```
==========================================================================
                          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 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   9.637 MF    0.6902 1.10418e4   266.61862  85.0570
   2  11.082 FM    0.7567 1939.85461   42.72510  14.9430

Totals :                  1.29817e4   309.34372
```

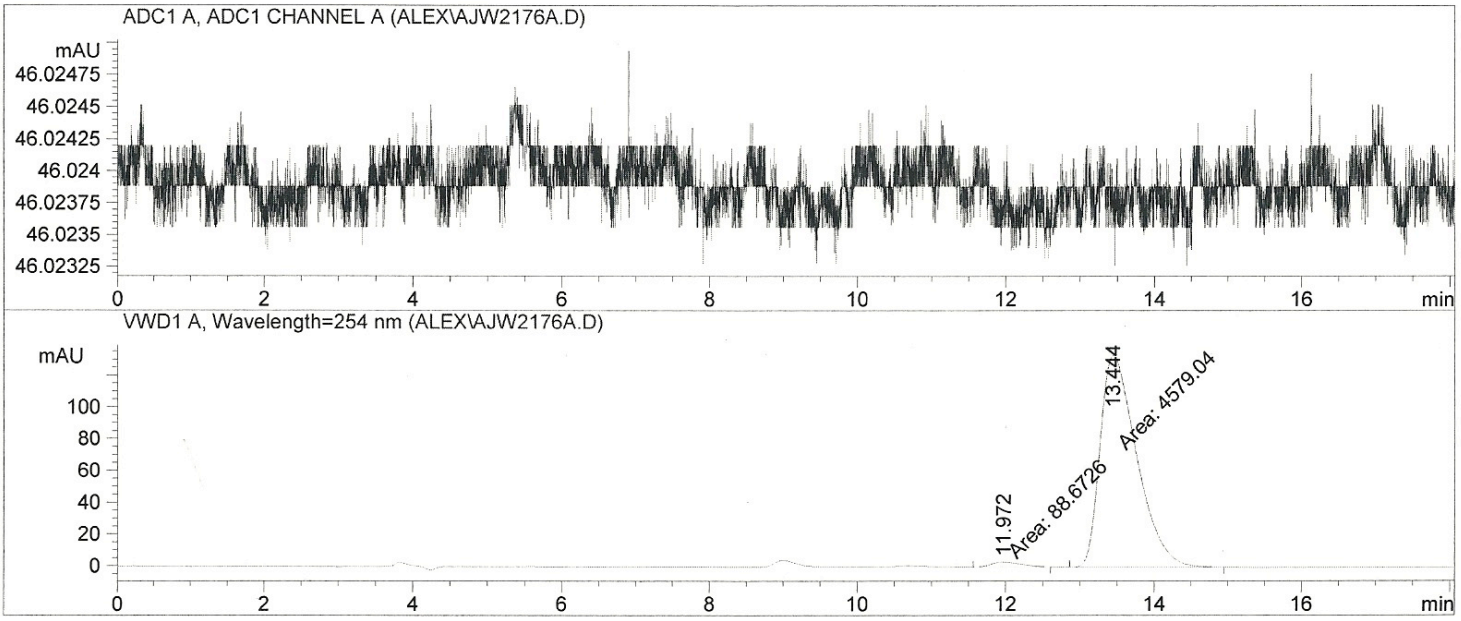
5% iPr/Hexanes on AD with AD guard 10 microL injection

```
==========================================================================
Injection Date  : 3/9/2012 2:18:48 PM
Sample Name     : AJW-2-40A4                        Location : Vial 3
Acq. Operator   : Alex
                                                    Inj Volume : 10 µl
Acq. Method     : C:\HPCHEM\1\METHODS\ALEX.M
Last changed    : 3/9/2012 12:49:39 PM by Alex
                  (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\ALEX.M
Last changed    : 3/9/2012 2:22:25 PM by Alex
                  (modified after loading)
==========================================================================
```




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

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :     10.00000  [ng/ul]    (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: ADC1 A, ADC1 CHANNEL A


Signal 2: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  12.038 MF    0.4986 7943.62842  265.53699  49.8658
   2  13.557 FM    0.5909 7986.37891  225.27487  50.1342

Totals :                  1.59300e4   490.81186

 Results obtained with enhanced integrator!
==========================================================================
                          Summed Peaks Report
==========================================================================

Signal 1: ADC1 A, ADC1 CHANNEL A
```

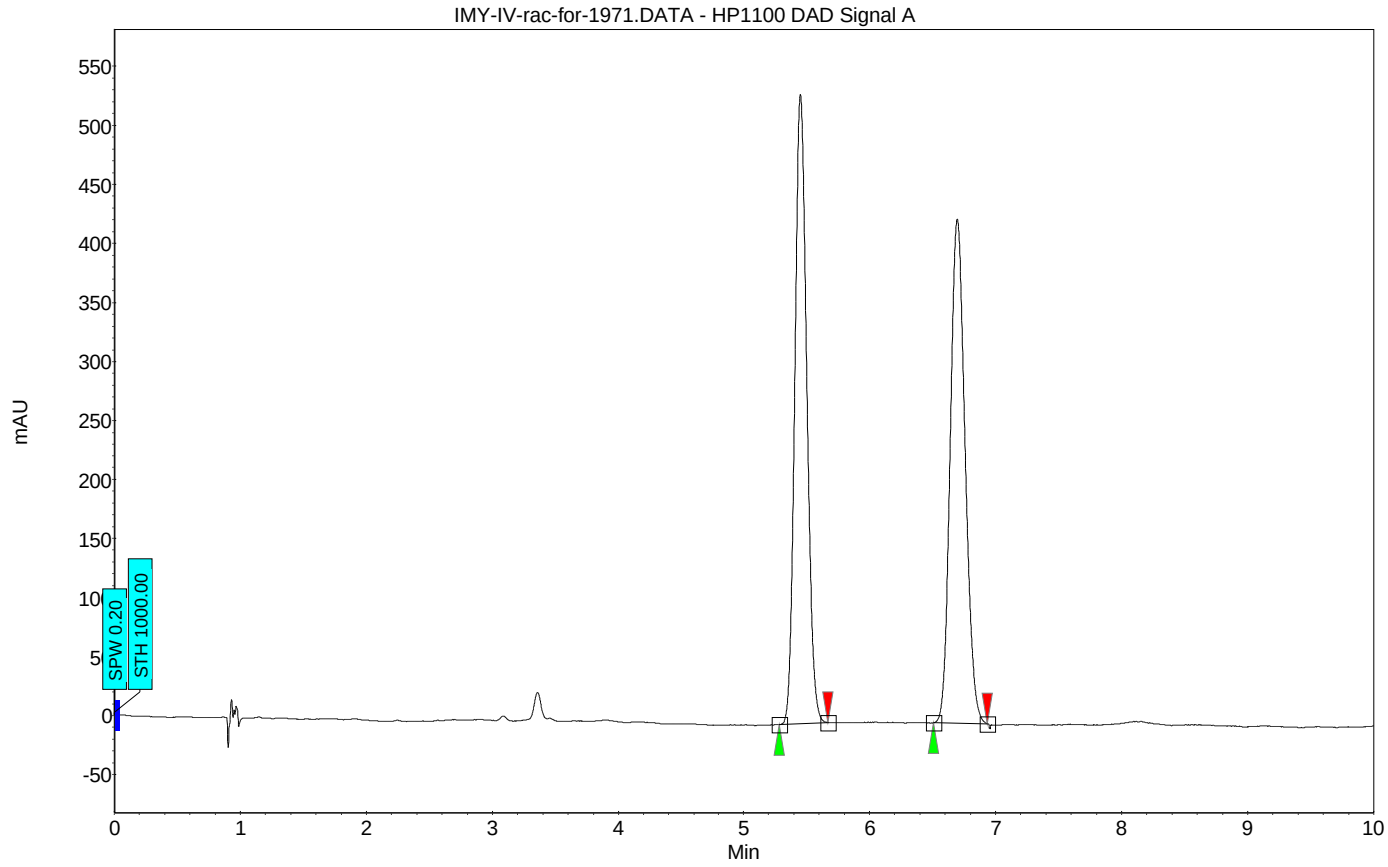
```
==========================================================================
Injection Date  : 3/9/2012 1:53:06 PM
Sample Name     : AJW-2-176A4                    Location : Vial 4
Acq. Operator   : Alex
                                                 Inj Volume : 10 µl
Acq. Method     : C:\HPCHEM\1\METHODS\ALEX.M
Last changed    : 3/9/2012 12:49:39 PM by Alex
                  (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\ALEX.M
Last changed    : 12/13/2011 8:09:06 PM by Alex
==========================================================================
```




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

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :     10.00000  [ng/ul]    (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: ADC1 A, ADC1 CHANNEL A


Signal 2: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  11.972 MM    0.4641   88.67263    3.18407   1.8997
   2  13.444 MM    0.5731 4579.04443  133.17099  98.1003

Totals :                  4667.71706  136.35506

 Results obtained with enhanced integrator!
==========================================================================
                          Summed Peaks Report
==========================================================================

Signal 1: ADC1 A, ADC1 CHANNEL A
```

Method Name:IMY-6-OMeNapEt-alcohol
Run Name:IMY-IV-rac-for-1971

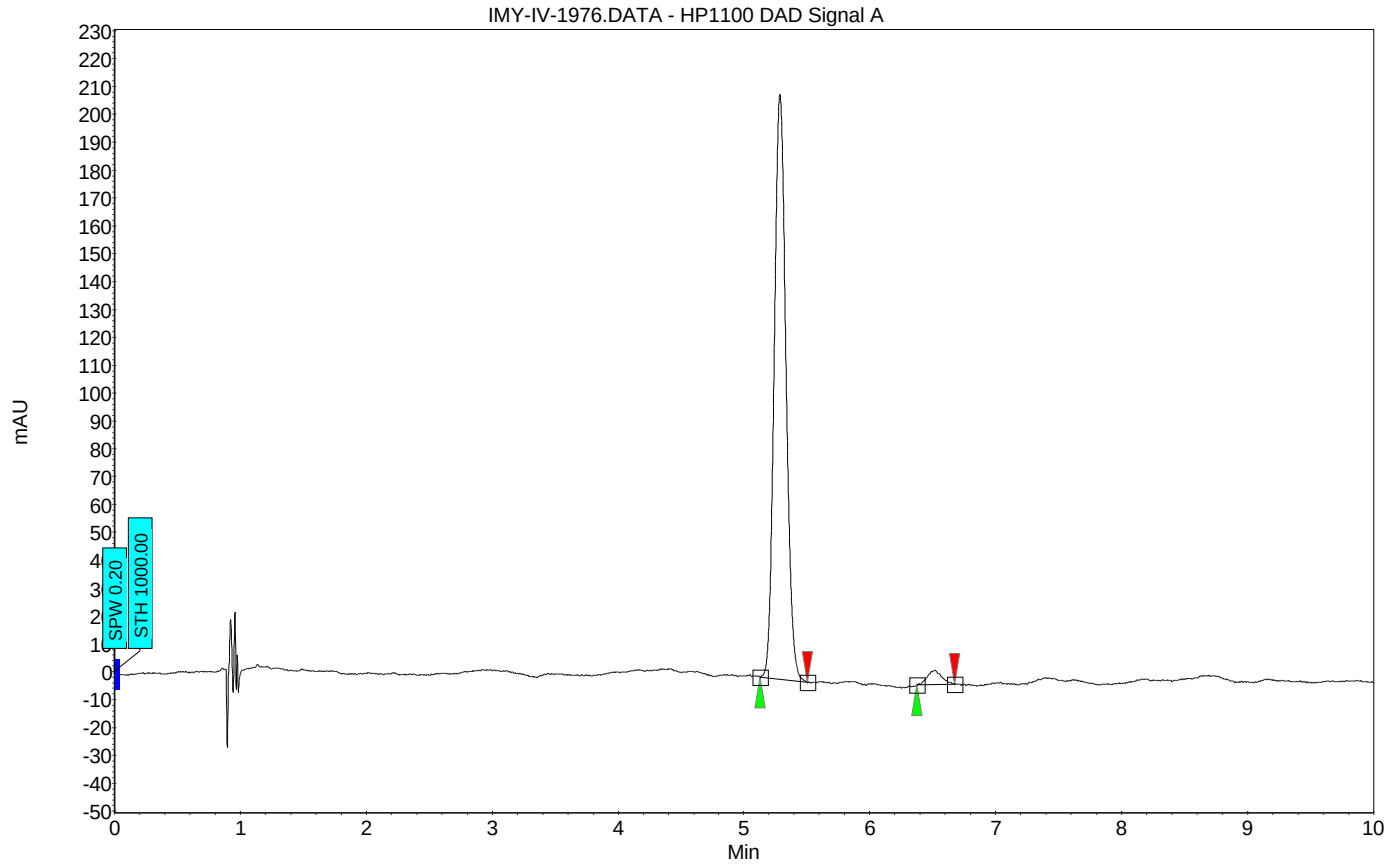
Date:2/25/2013
Time:5:07:26 PM



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	5.28	5.45	5.67	0.00	50.08	533.2	58.7	50.078
2	UNKNOWN	6.51	6.69	6.93	0.00	49.92	427.1	58.5	49.922
Total						100.00	960.2	117.1	100.000

Method Name:IMY-6-OMeNapEt-alcohol
Run Name:IMY-IV-1976

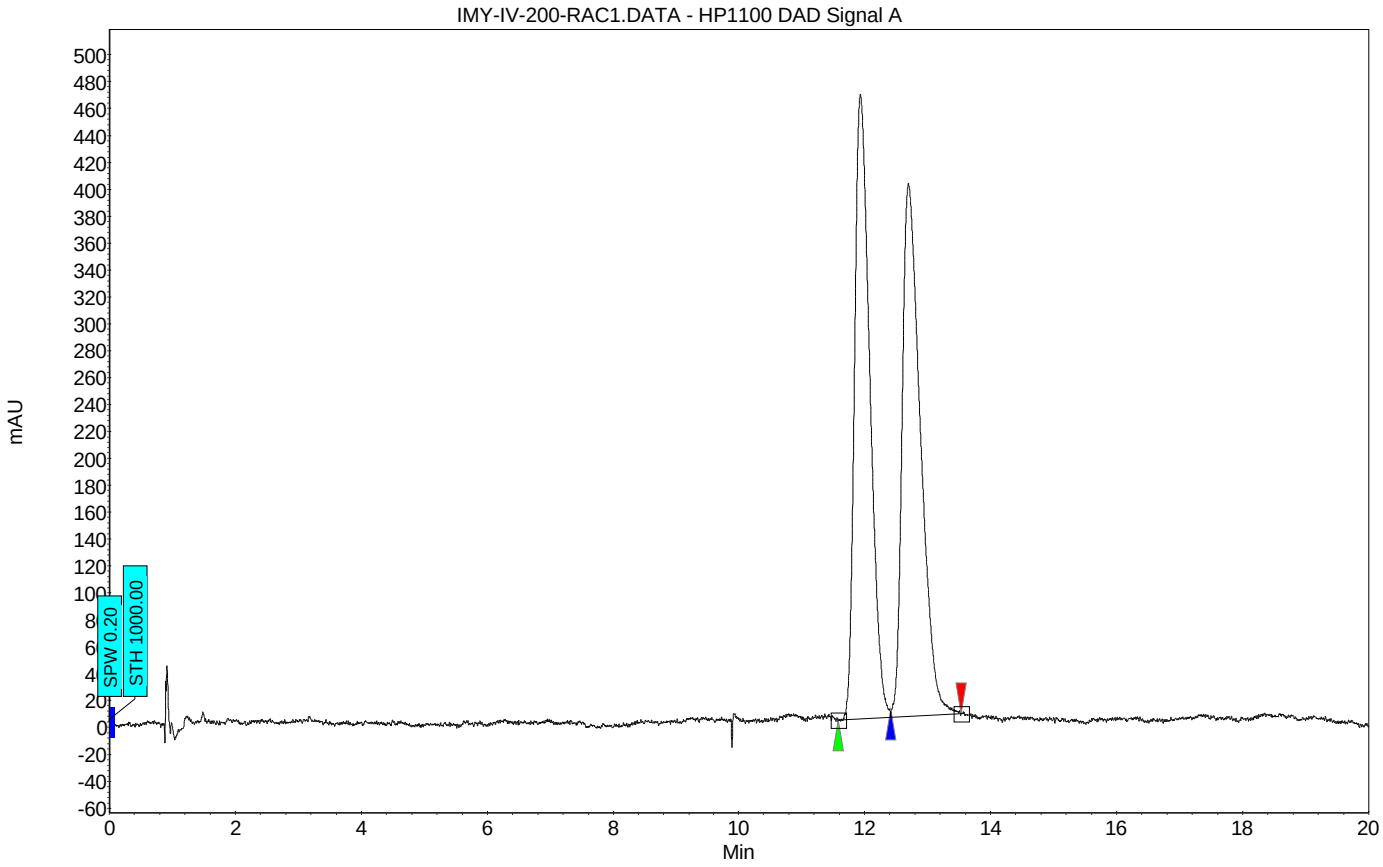
Date:2/25/2013
Time:5:05:59 PM



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	5.13	5.29	5.51	0.00	97.12	209.9	22.7	97.119
2	UNKNOWN	6.38	6.52	6.67	0.00	2.88	5.2	0.7	2.881
Total						100.00	215.0	23.4	100.000

Method Name:AGJ-nap-cyclohex_OH
Run Name:IMY-IV-200-RAC1

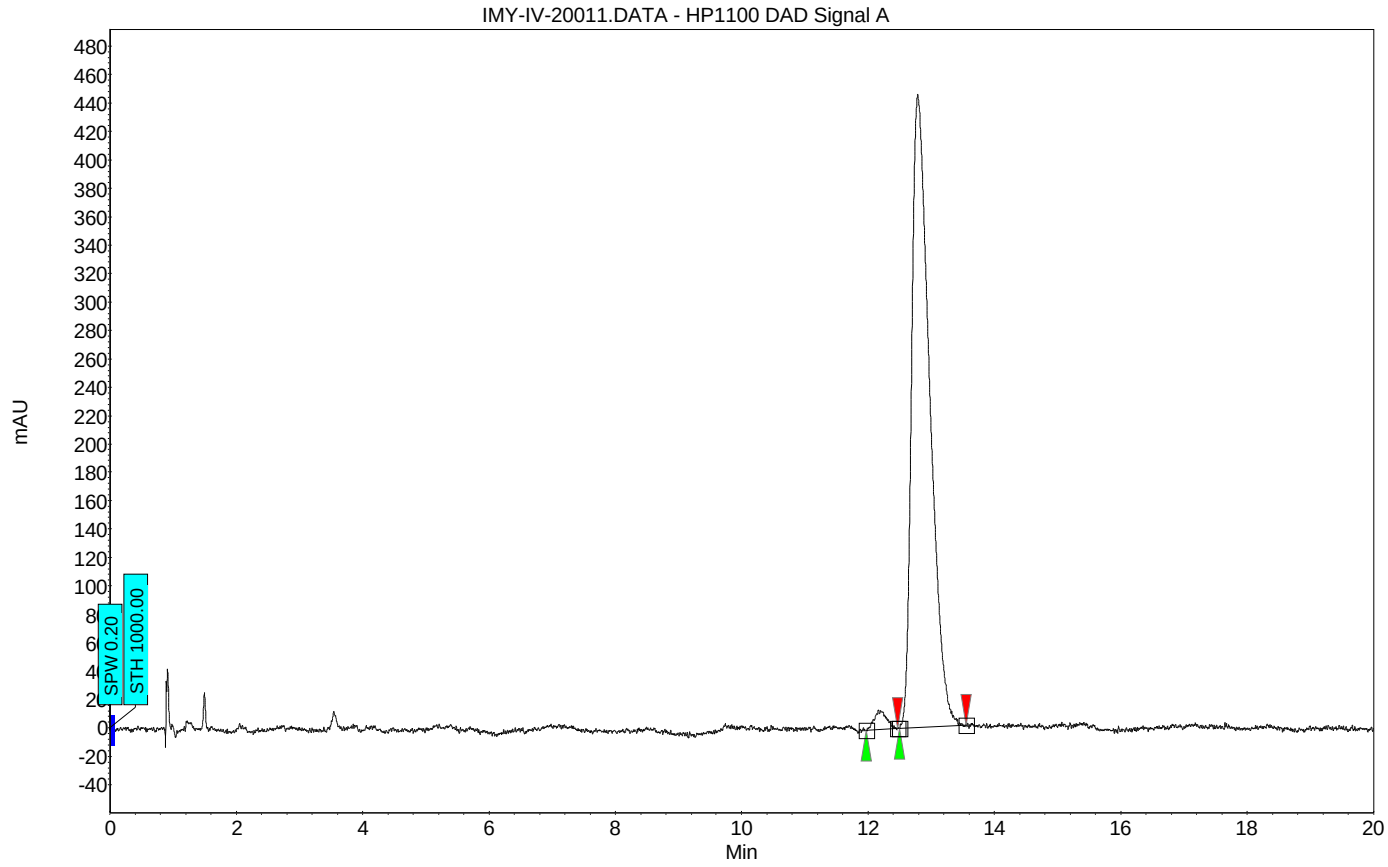
Date:2/25/2013
Time:5:08:40 PM



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	11.58	11.93	12.41	0.00	49.52	464.2	131.0	49.517
2	UNKNOWN	12.41	12.69	13.53	0.00	50.48	396.3	133.6	50.483
Total						100.00	860.5	264.6	100.000

Method Name:AGJ-nap-cyclohex_OH
Run Name:IMY-IV-20011

Date:2/25/2013
Time:5:08:07 PM



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	11.98	12.17	12.47	0.00	2.01	13.9	3.0	2.010
2	UNKNOWN	12.50	12.79	13.55	0.00	97.99	445.8	147.3	97.990
Total						100.00	459.7	150.3	100.000