Supporting Information

Synthetic and Theoretical Investigation on One-Pot Halogenation of β-Amino Alcohols and Nucleophilic Ring Opening of Aziridinium Ions

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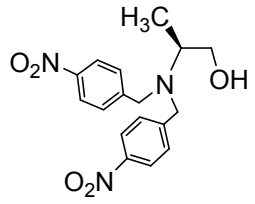
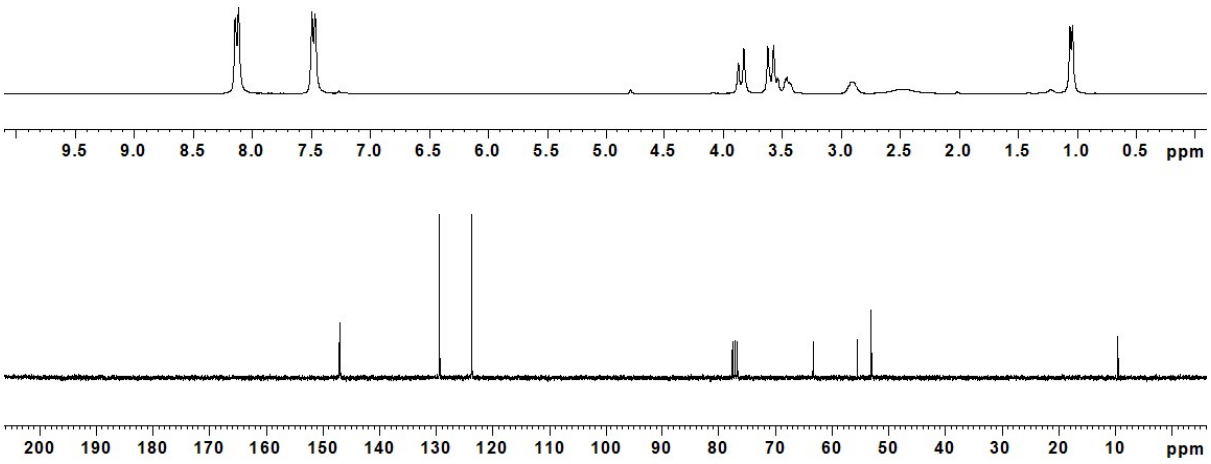
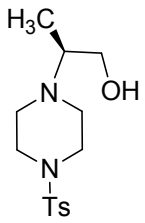
^{1}H and ^{13}C NMR Spectra of Compounds



(S)-1b





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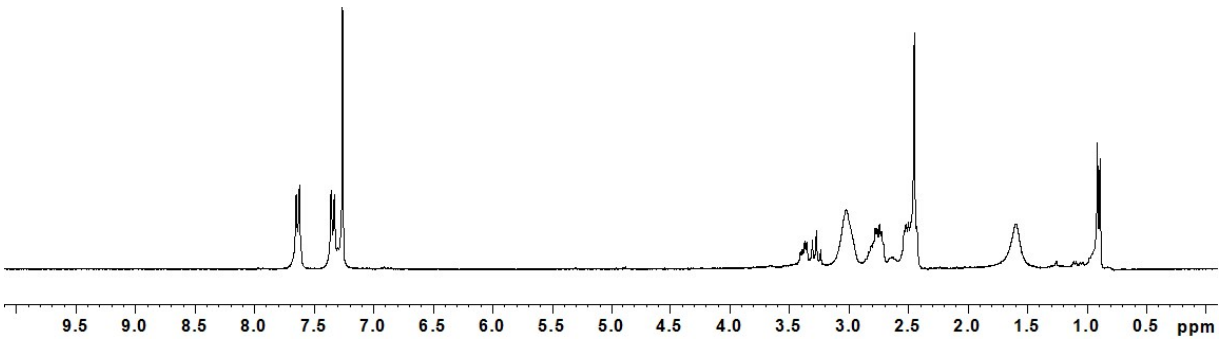
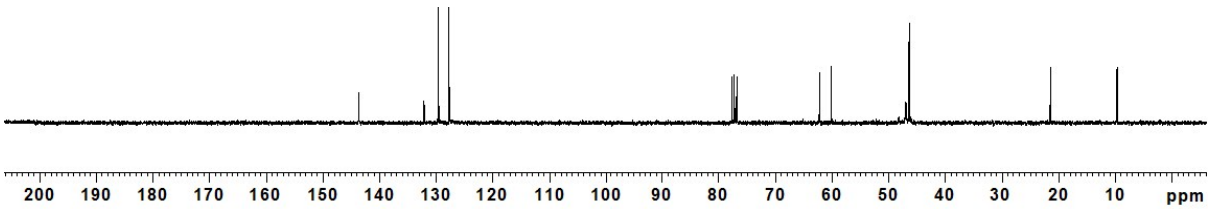
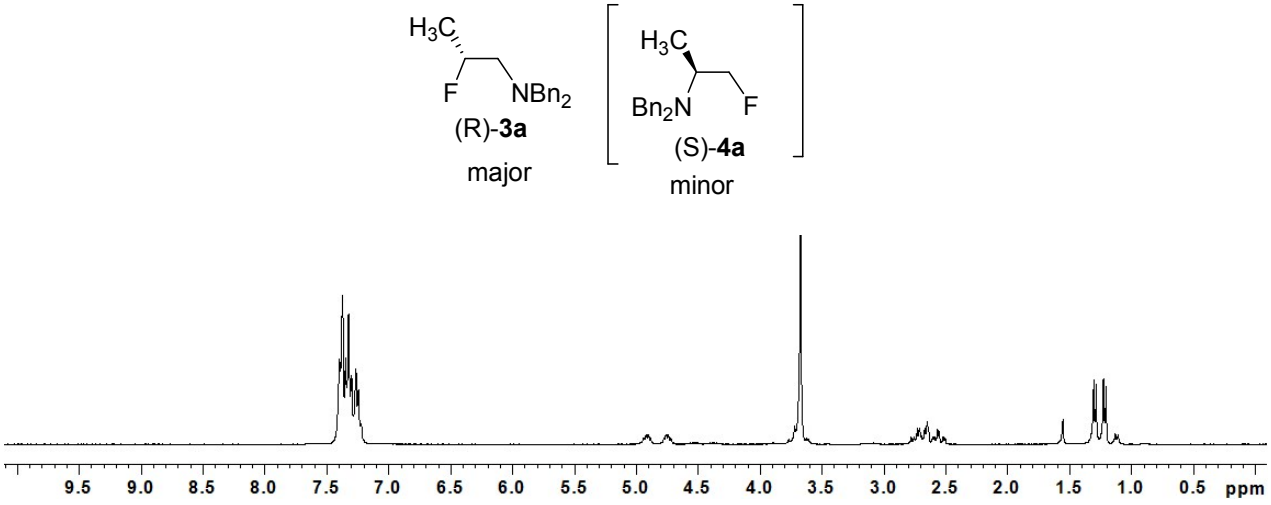
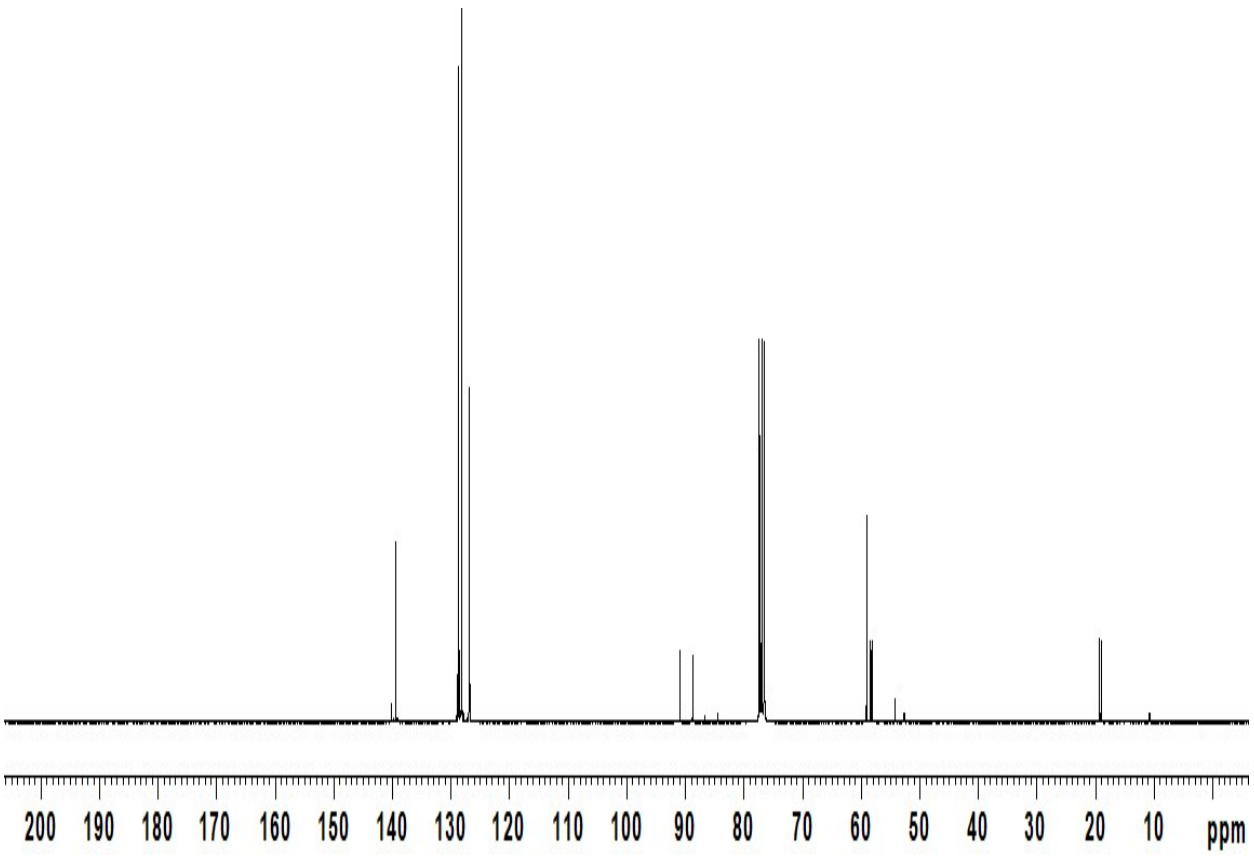





H3C
F
NBn2
(R)-3a
major
H3C
Bn2N
F
(S)-4a
minor
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm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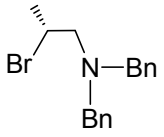
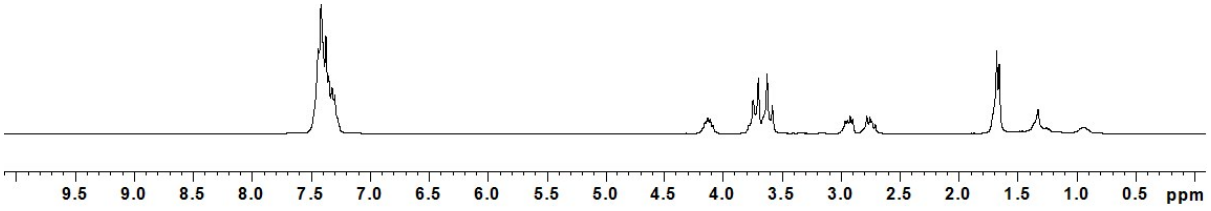
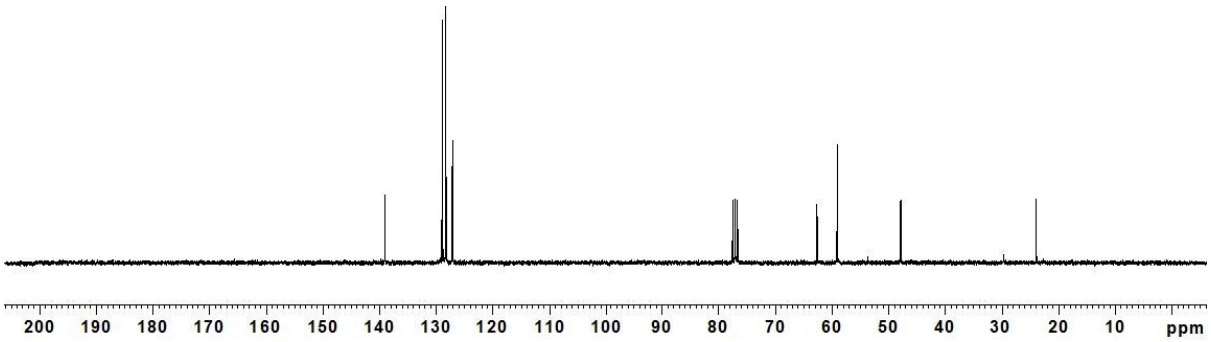
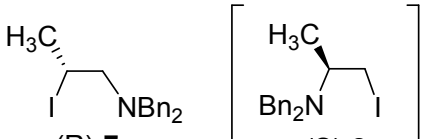


(R)-5b

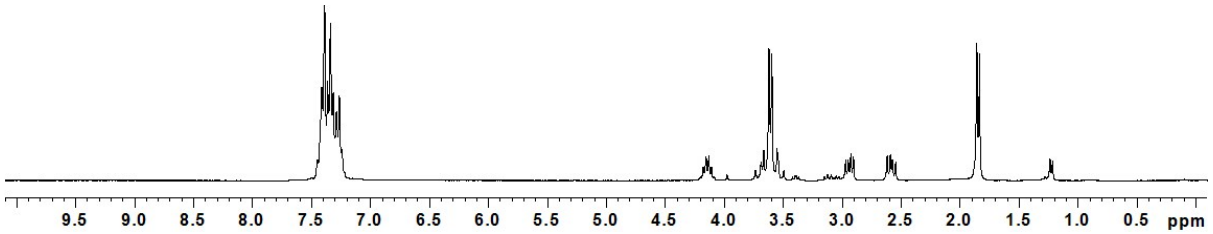


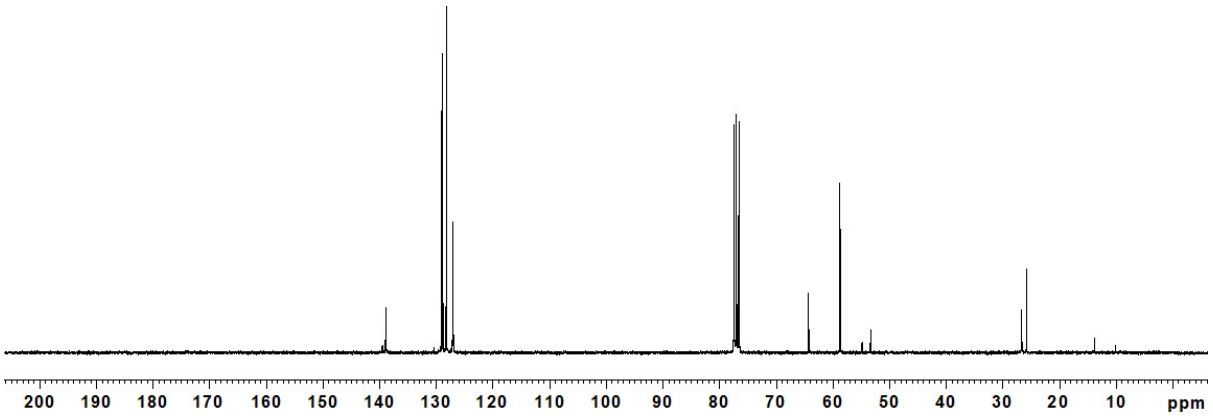


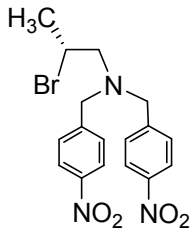


(R)-**7a**
major

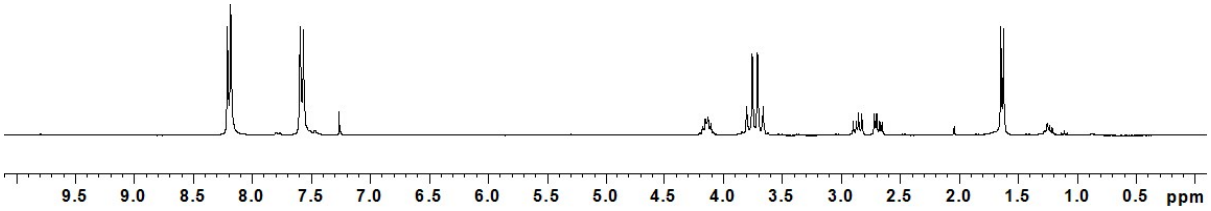
(S)-**8a**
minor

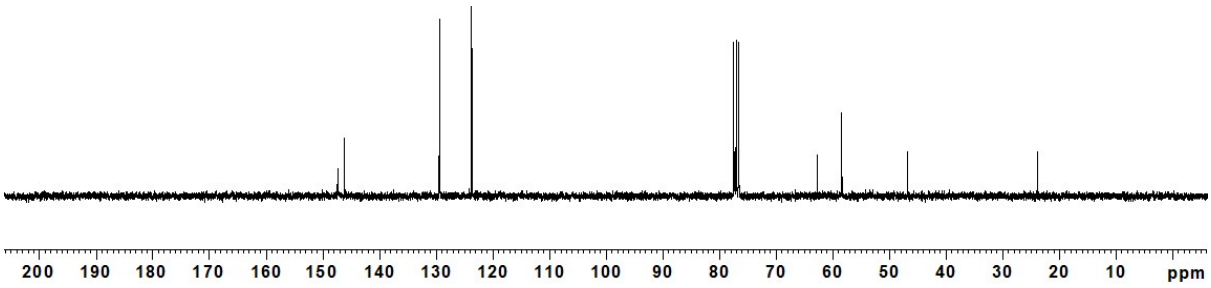





H3C
Br
N
NO2
NO2

(R)-**6b**


9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm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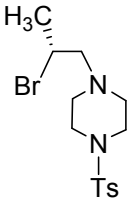
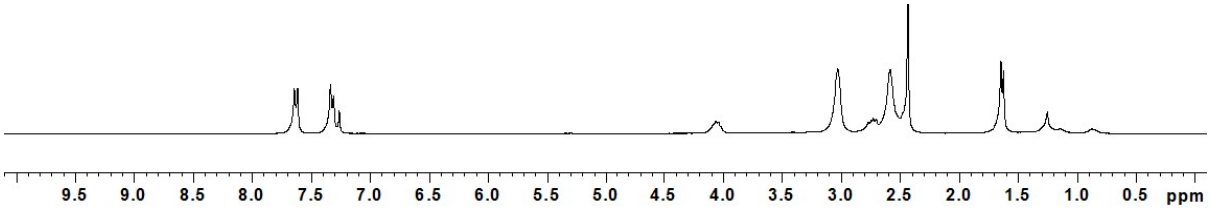

H3C
Br
N
N
Ts

(R)-**6c**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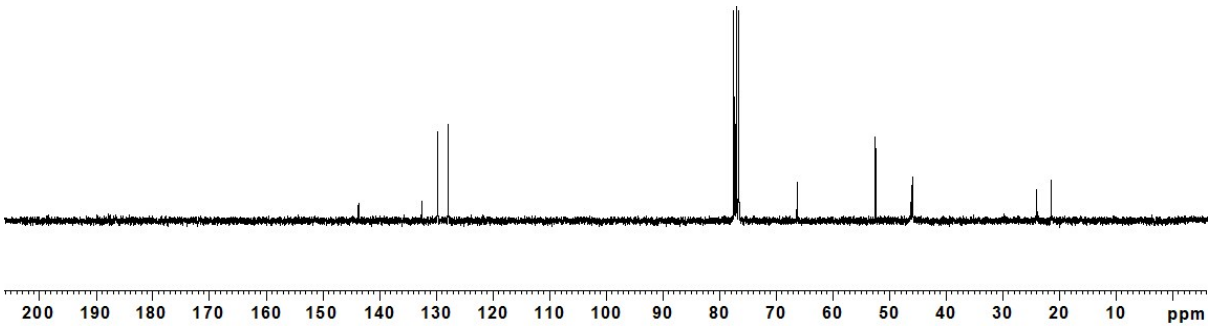
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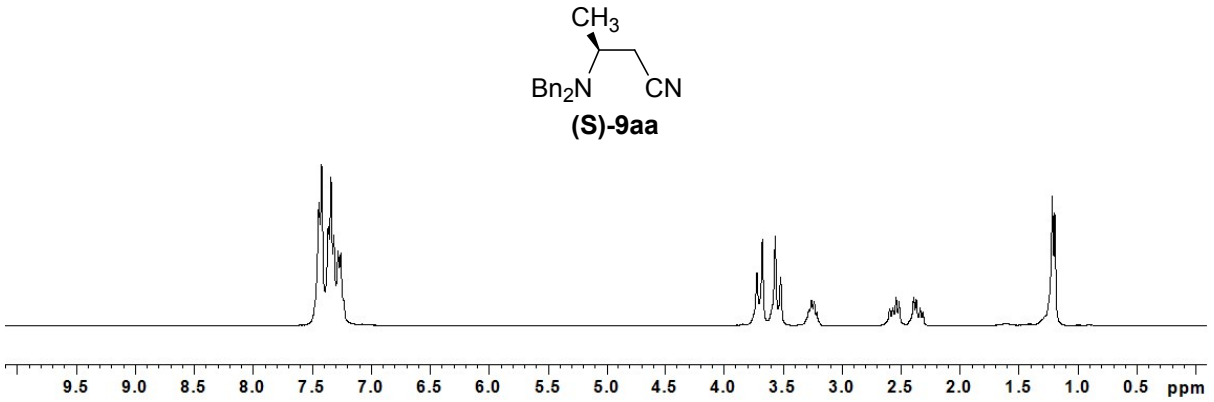
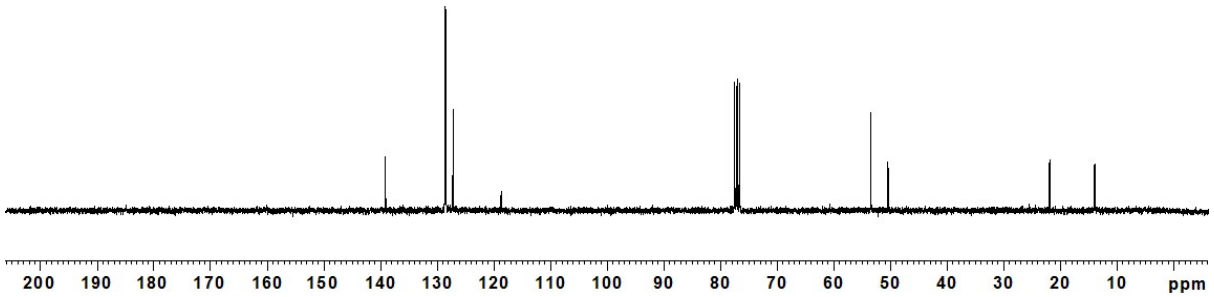
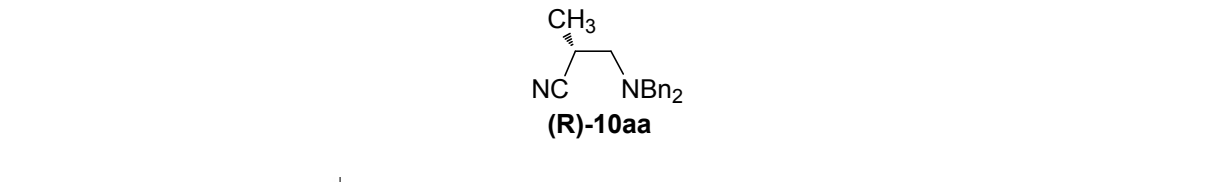
Table 2. Ring opening of aziridinium ions: synthesis of β-amino nitriles

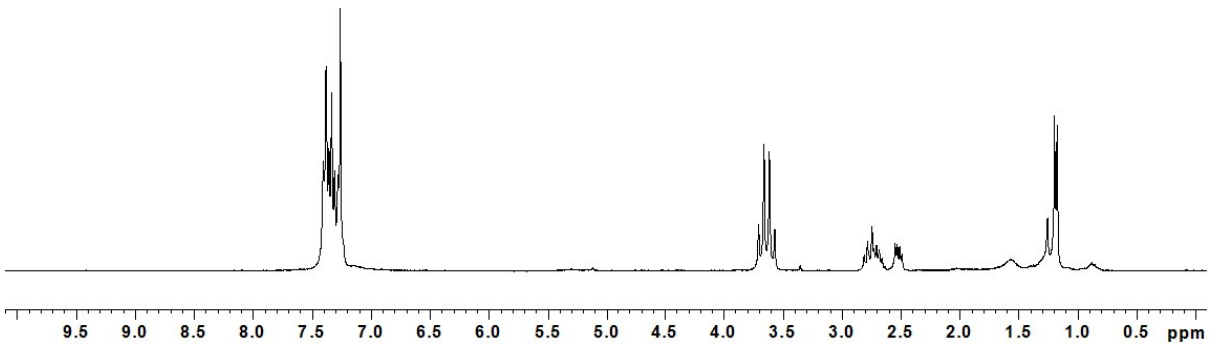


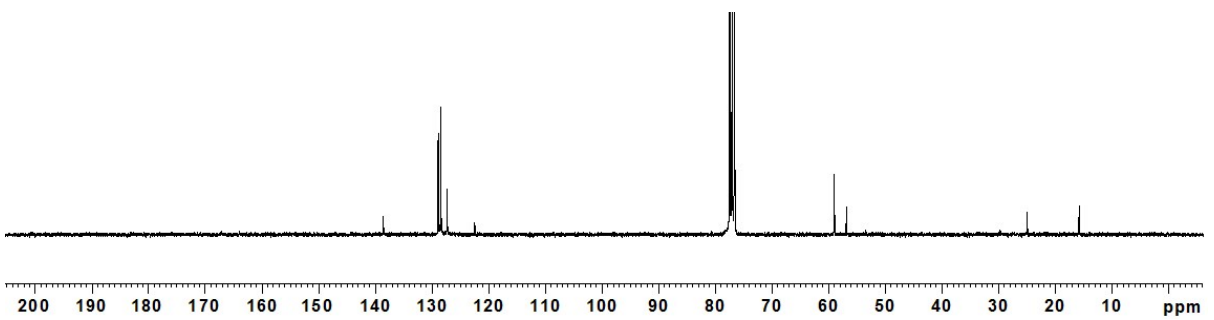
(S)-9aa

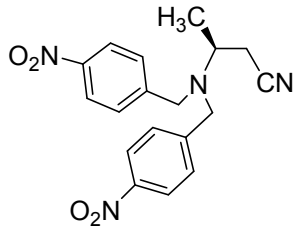




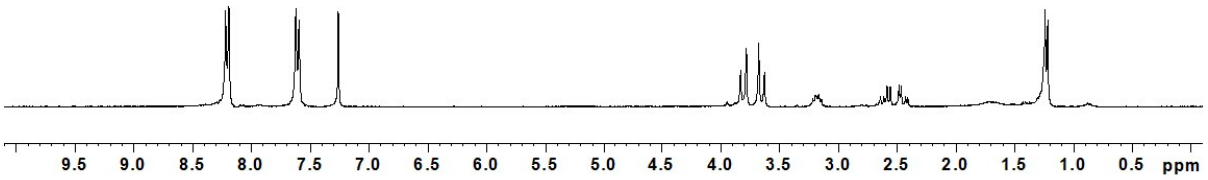
(R)-10aa

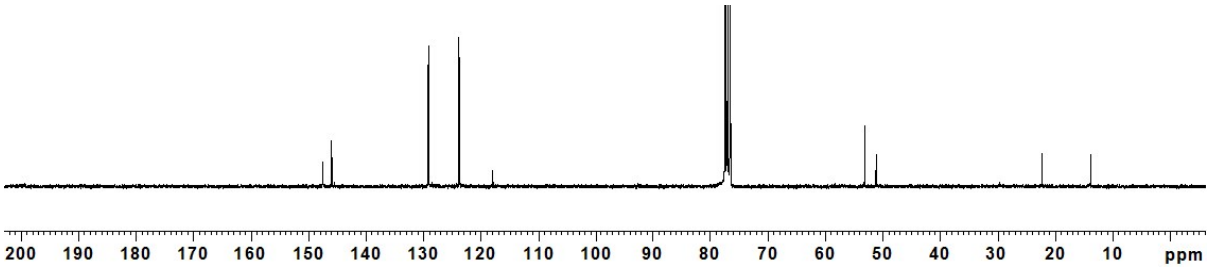





H3C
O2N
N
CN
O2N

(S)-9b


9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm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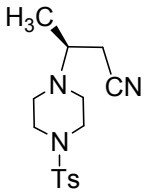
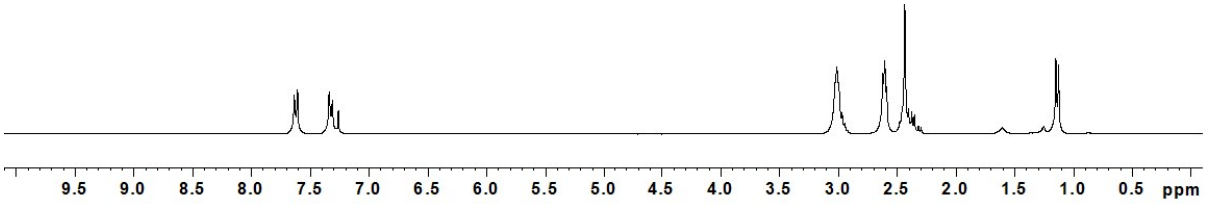

H3C
N
CN
N
Ts

(S)-9c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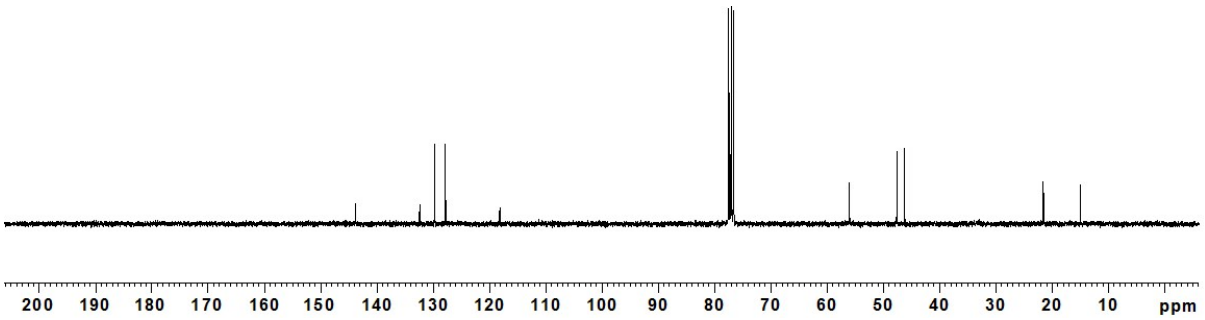
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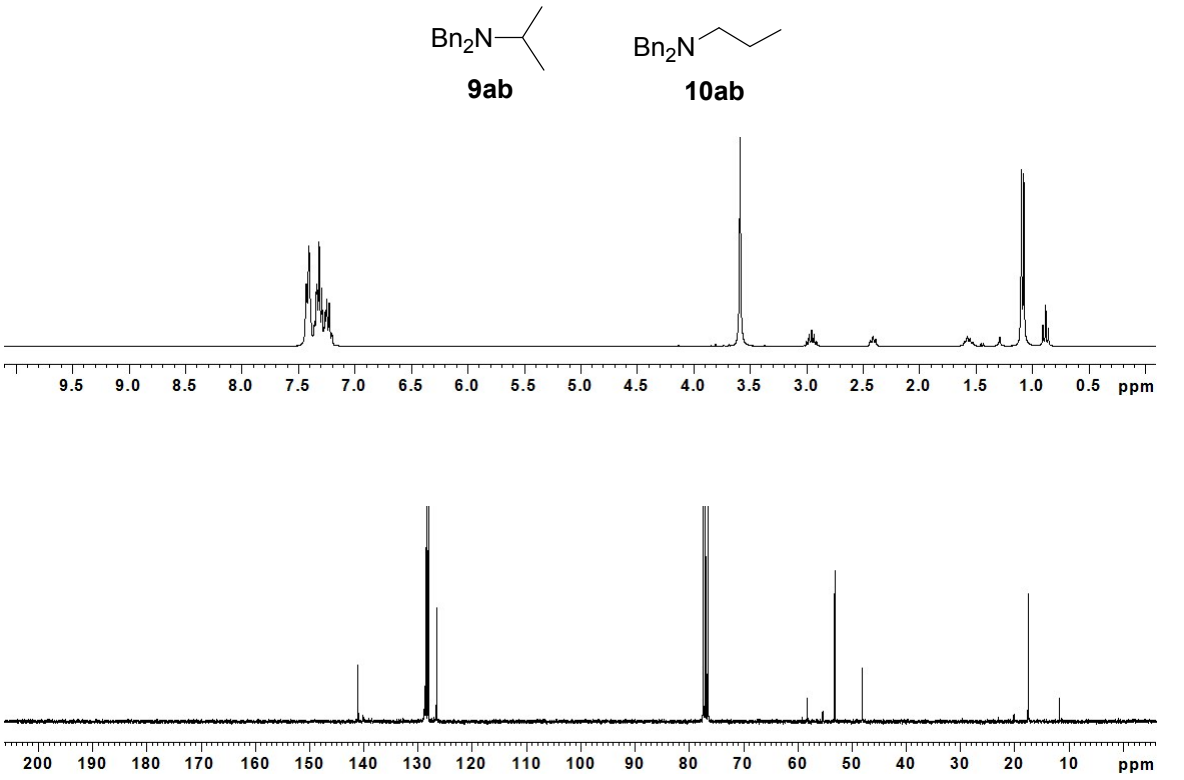
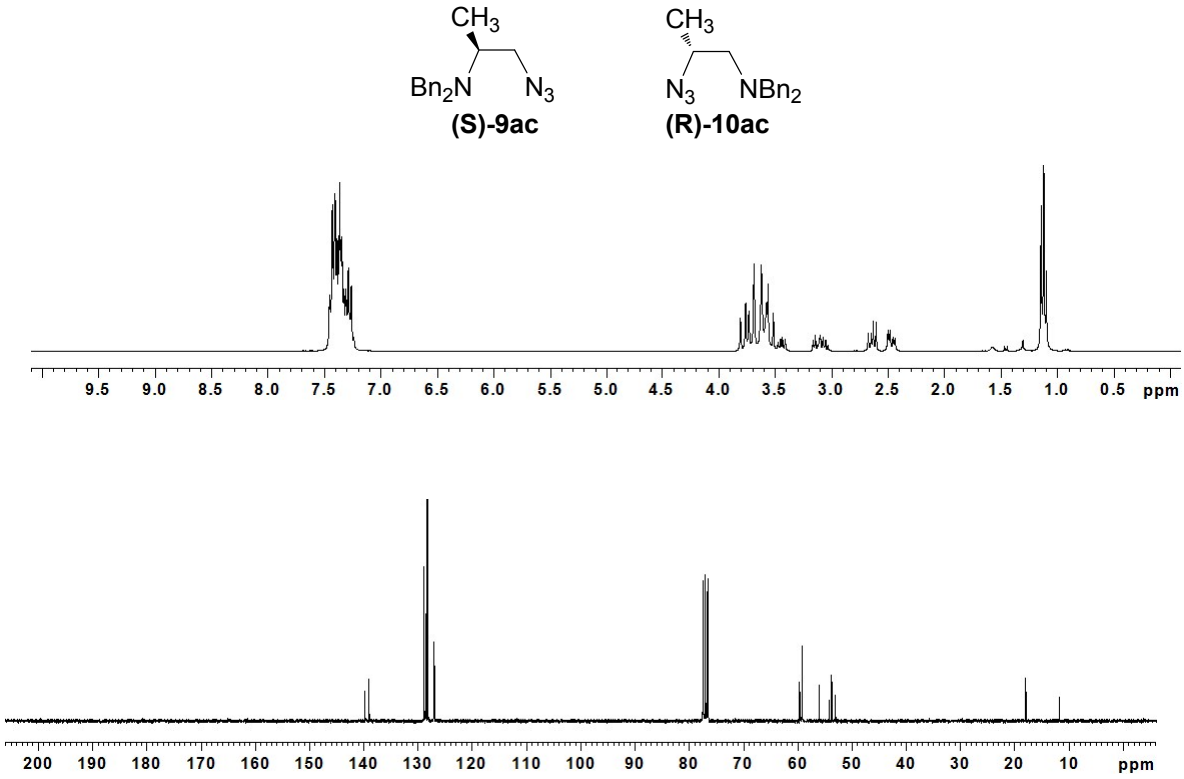
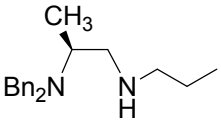
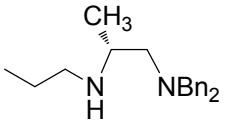
Table 3. Ring opening of aziridinium ion (S)-2a with different nucleophiles



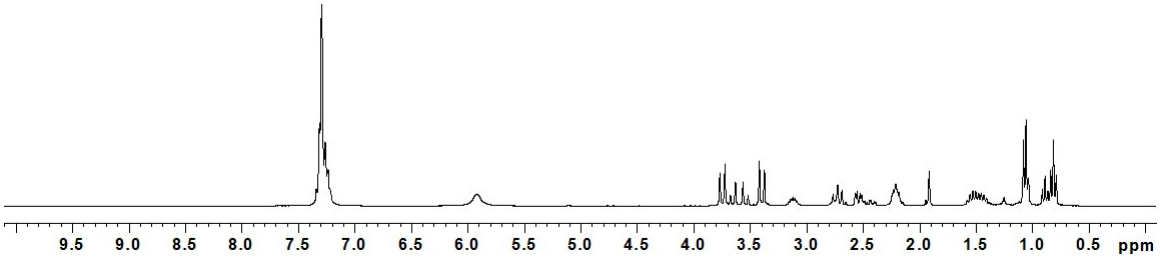


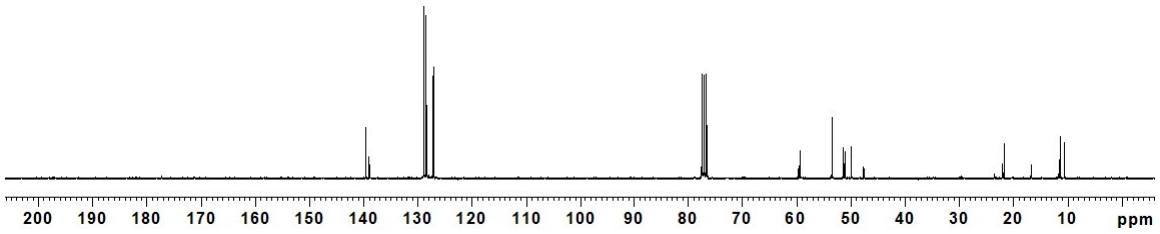


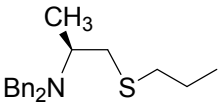
(S)-9ad



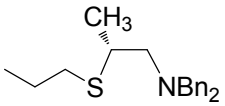
(R)-10ad







(S)-9ae



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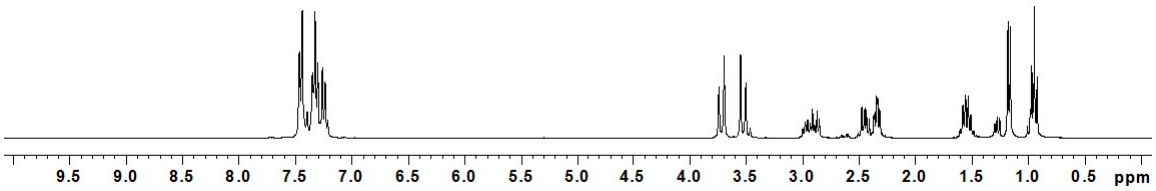
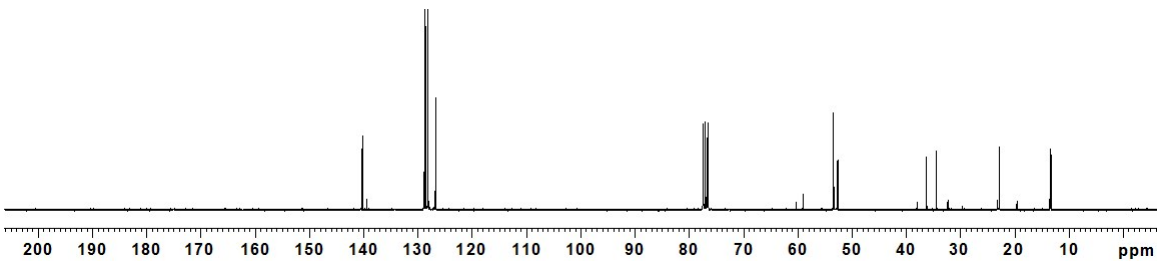
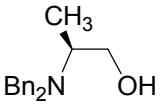
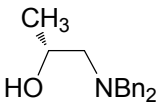




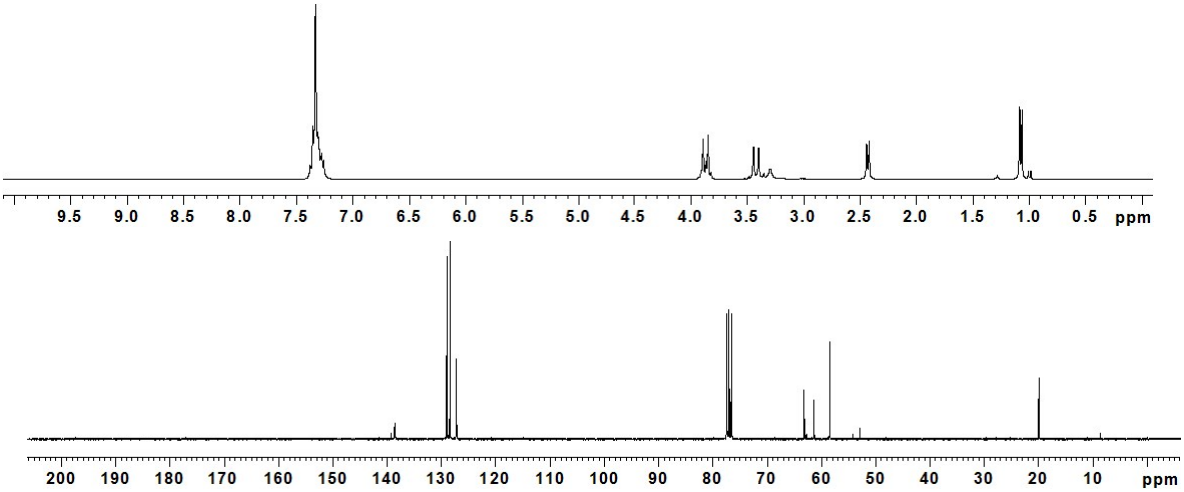


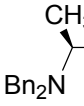
(S)-9af



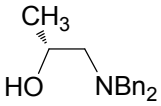
(R)-10af

(Table 3, entry 6, in the absence of NaOH)



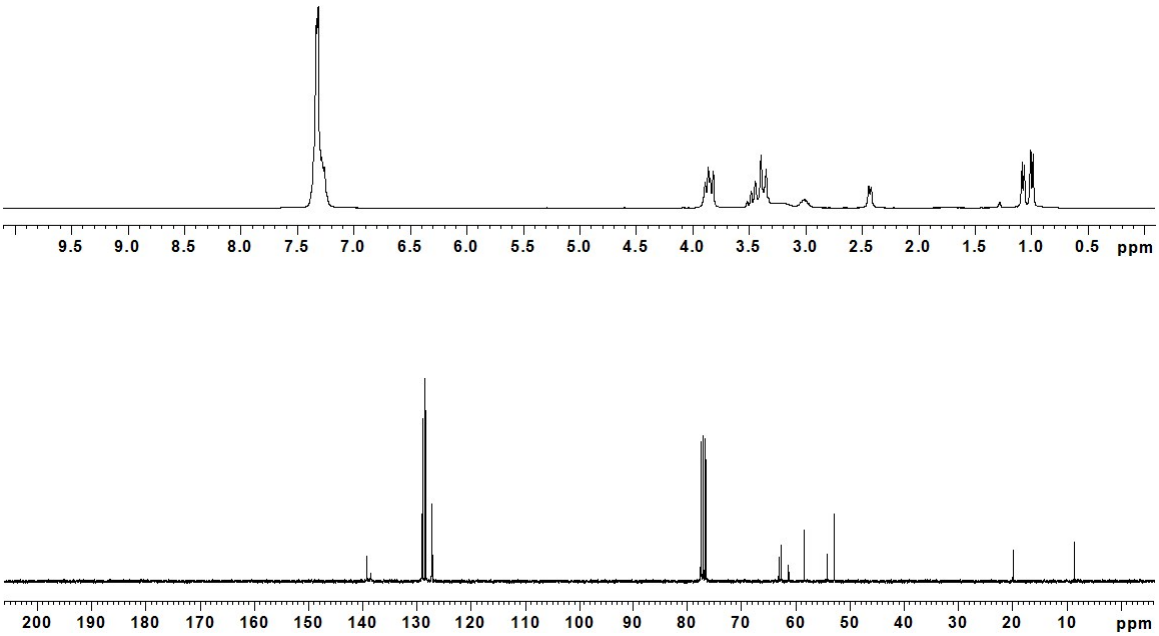


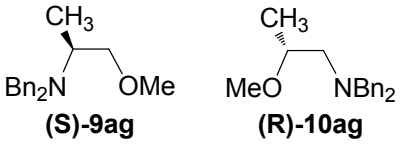
(S)-9af



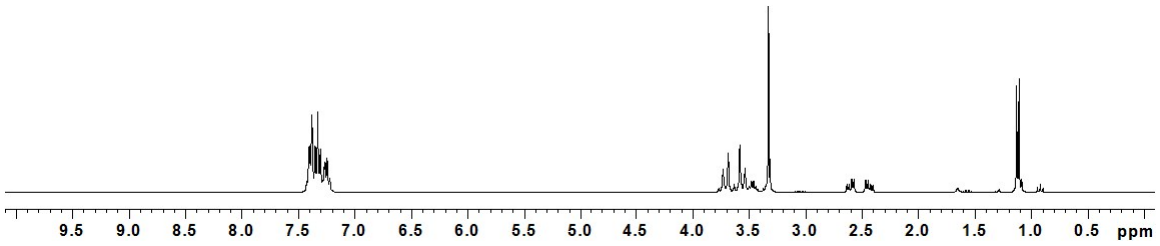
(R)-10af

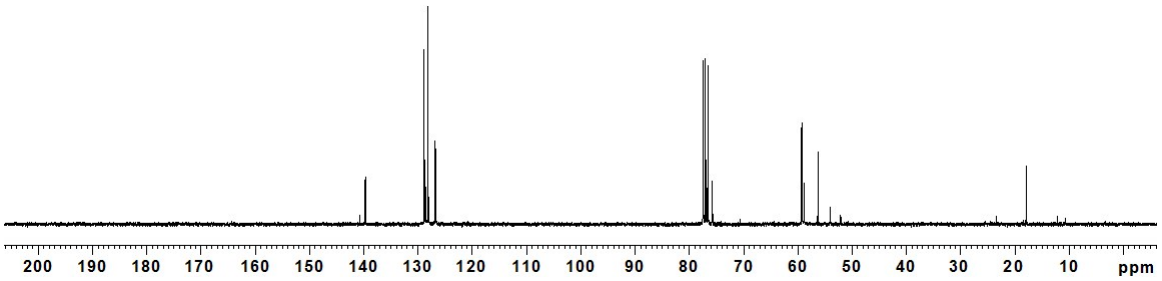
(Table 3, entry 9, in the presence of NaOH))

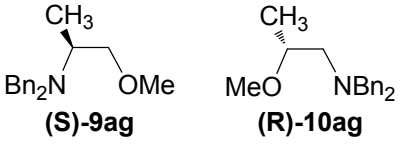




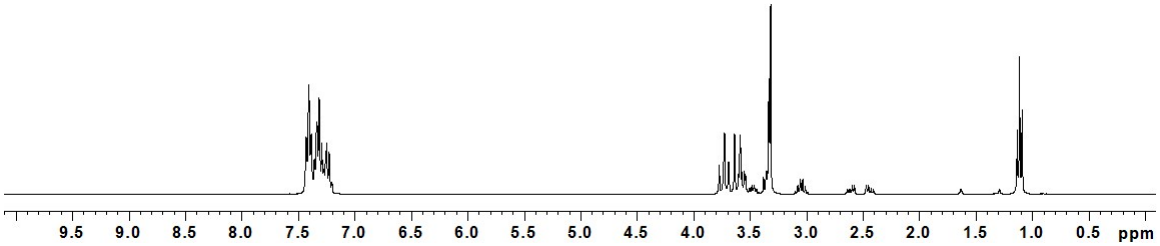
(S)-9ag **(R)-10ag** (Table 3, entry 7, in the absence of NaOH)

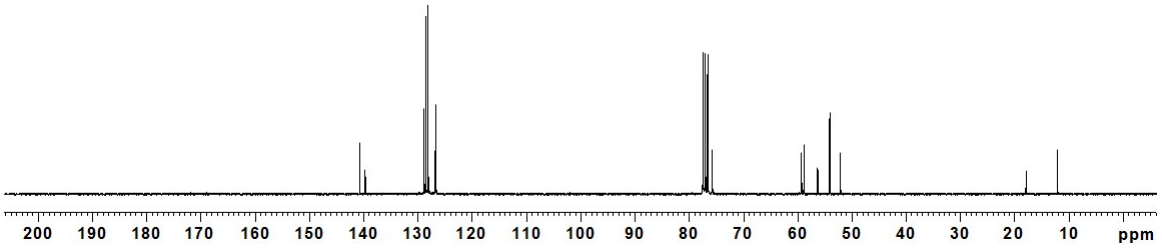


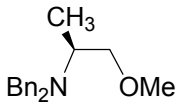




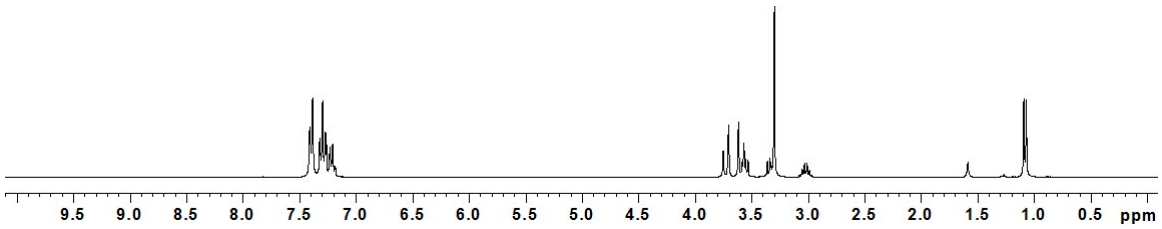
(S)-9ag **(R)-10ag** (Table 3, entry 10, in the presence of NaOH)

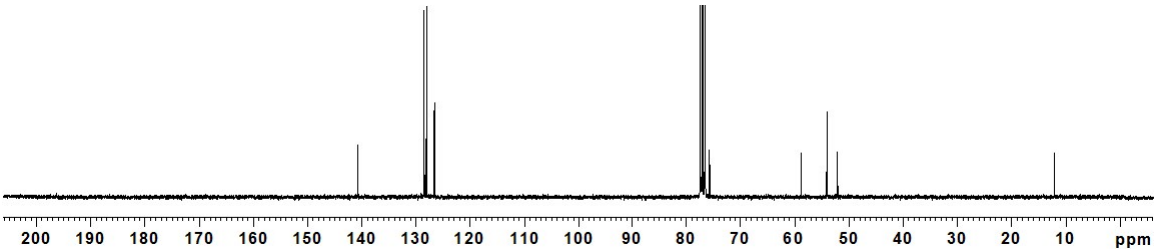


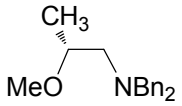



CH3
Bn2N
OMe

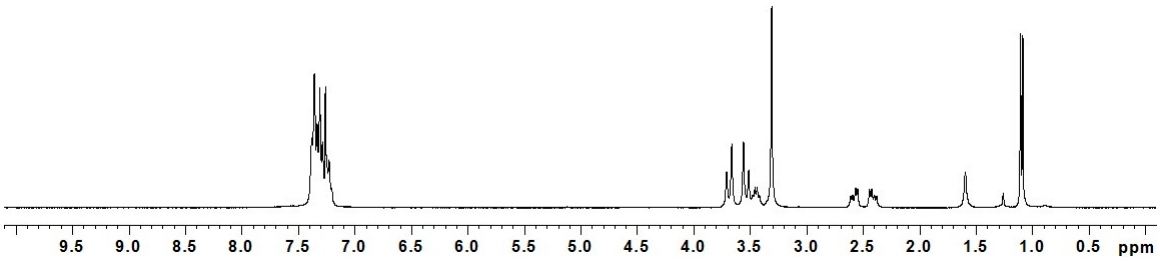
(S)-9ag

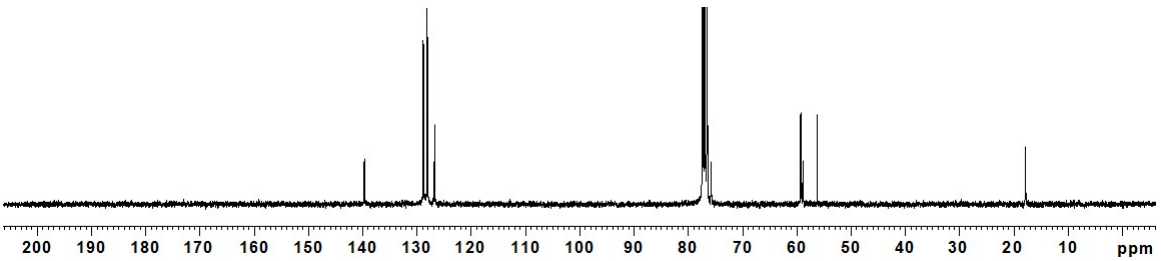

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


CH3
MeO
NBn2

(R)-10ag


9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

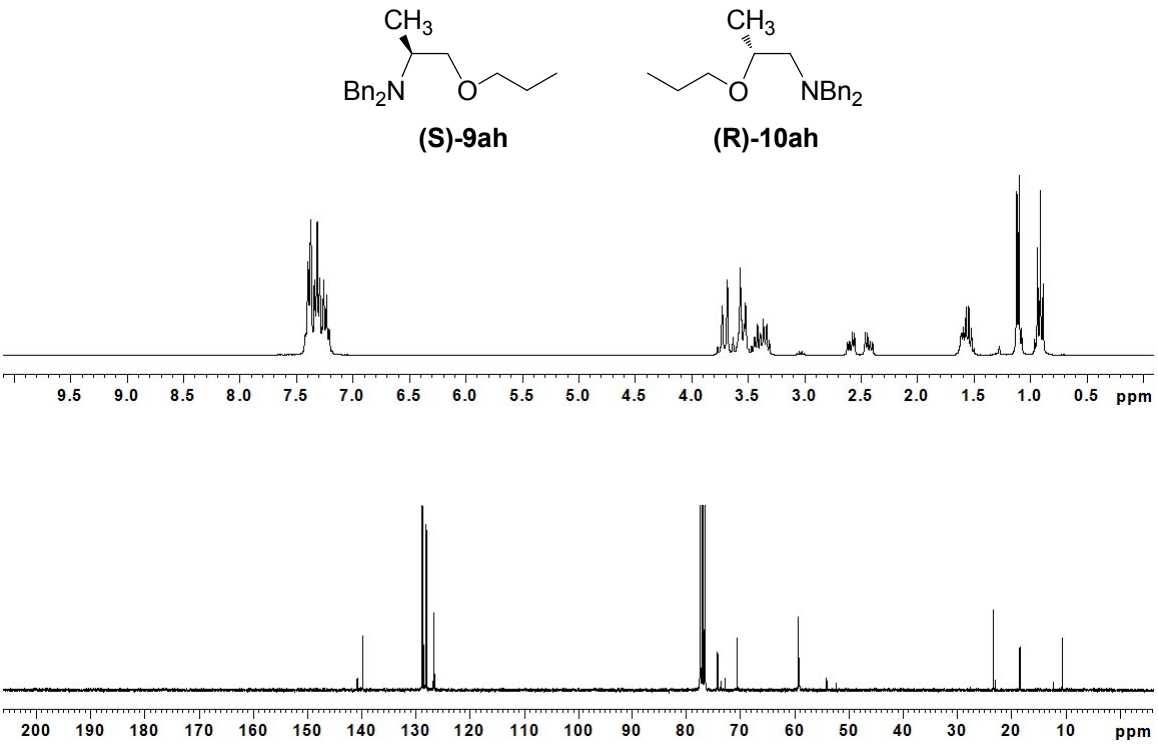
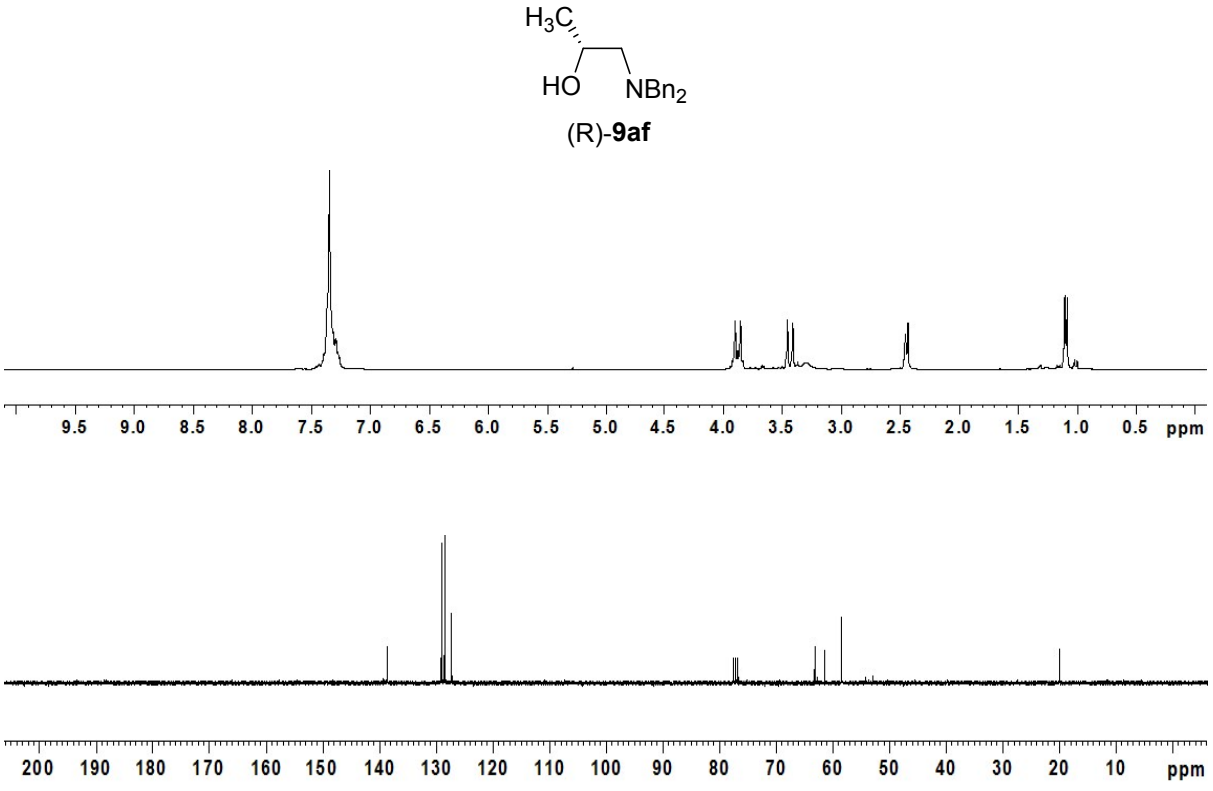
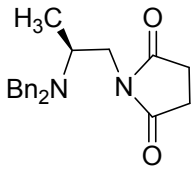
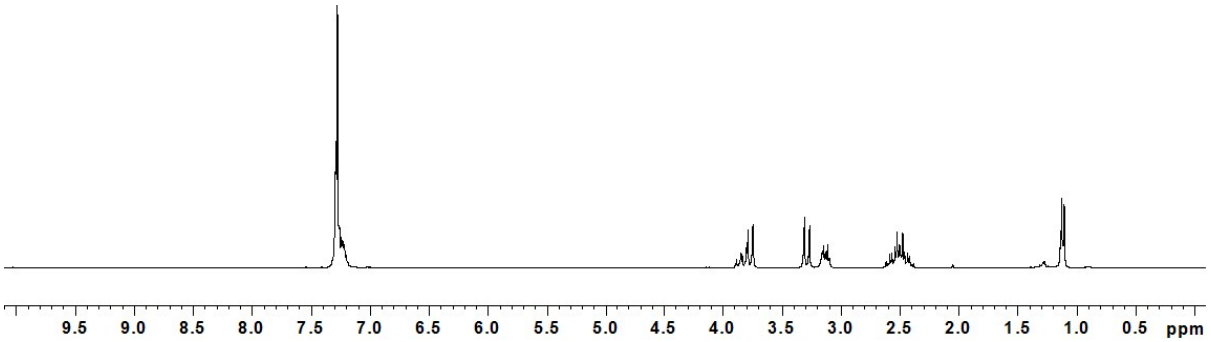


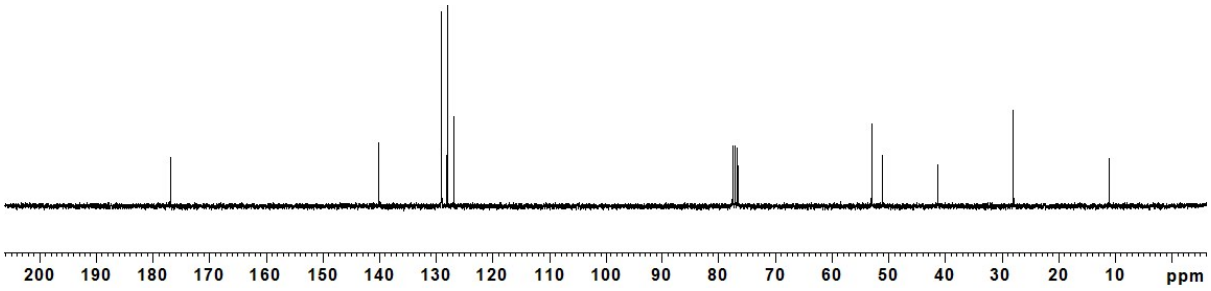
Table 4. One-pot synthesis of N-protected b-amino nitrile, β-amino alcohol, and vicinal diamine from primary β-amino alcohol (S)-1a.

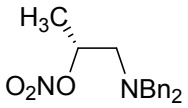



H3C
O
Bn2N
N
O

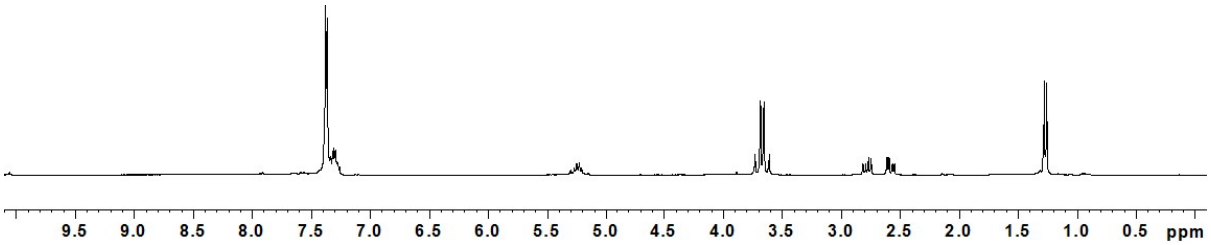
(S)-11

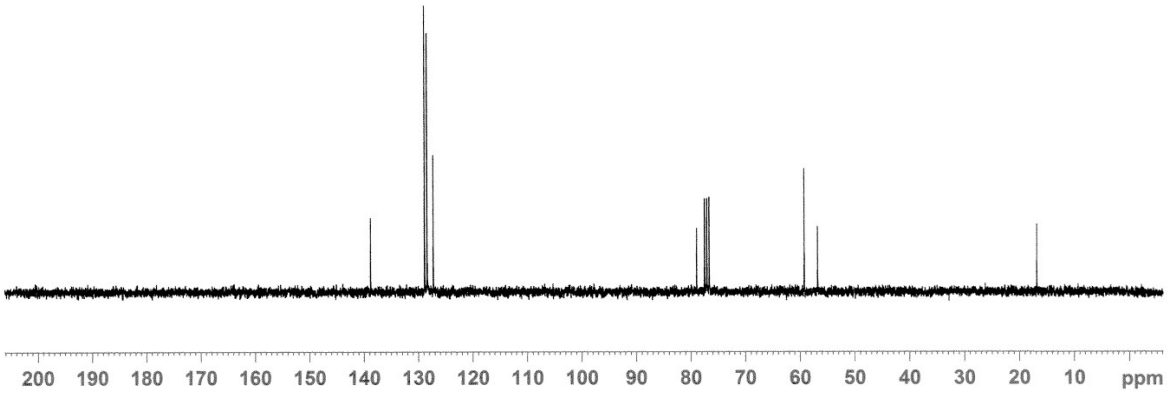

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

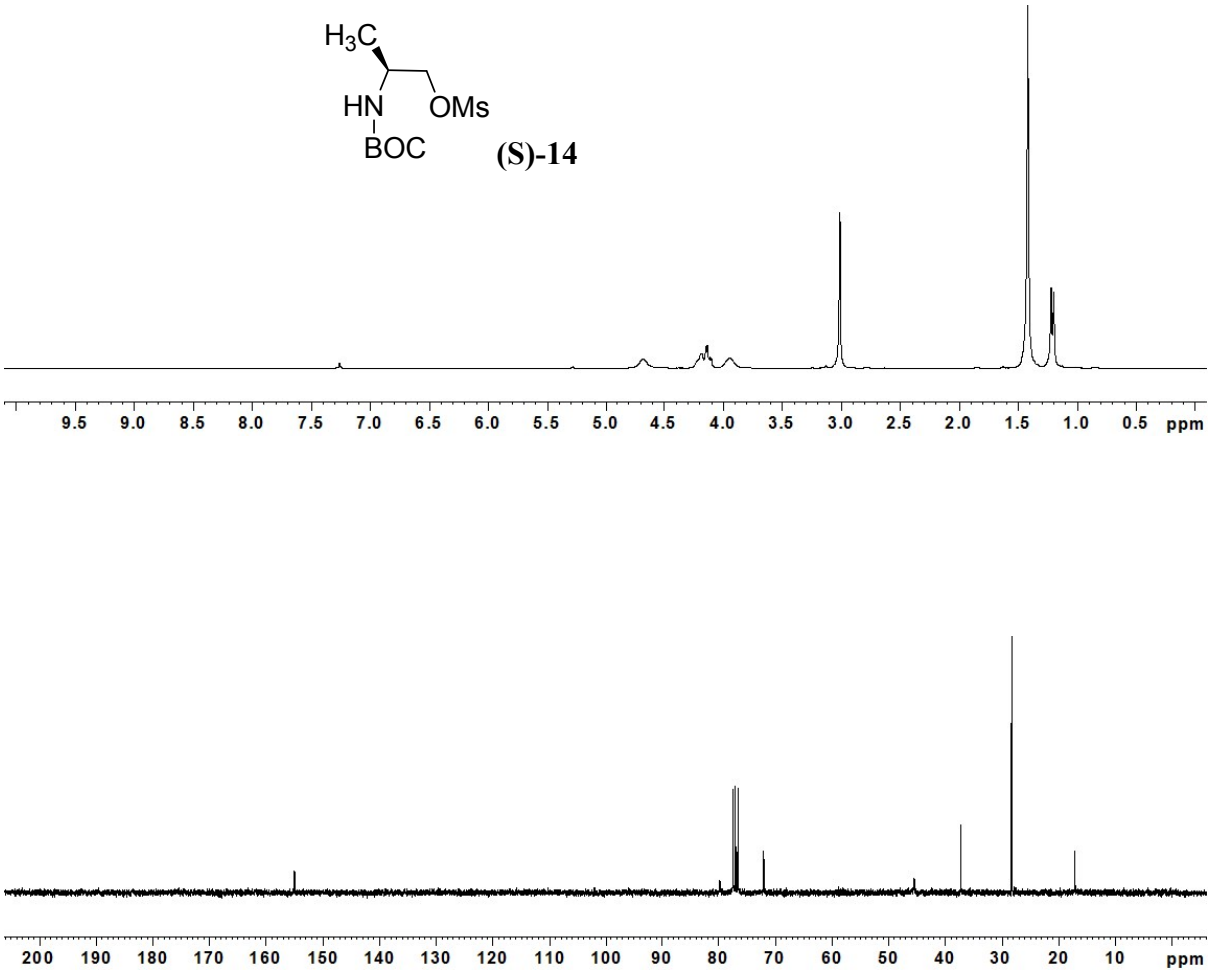

H3C
O2NO
NBn2

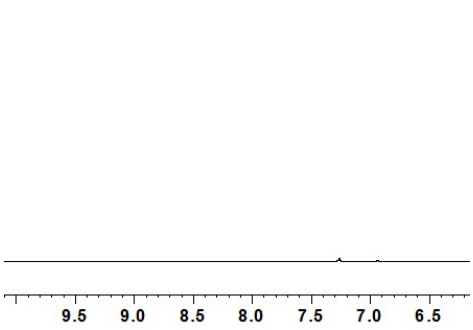
(R)-**12**

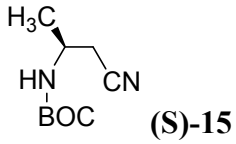

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

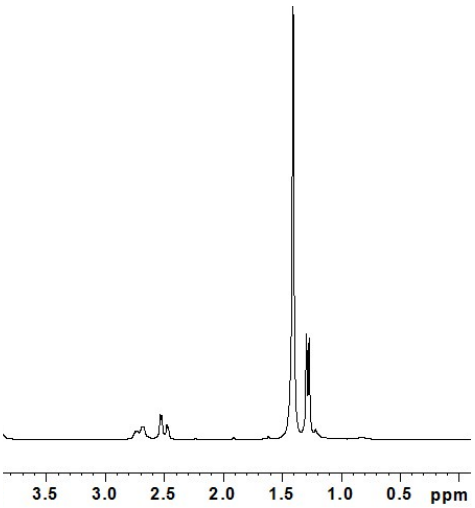
Scheme 3. Structural determination of 9aa and 11

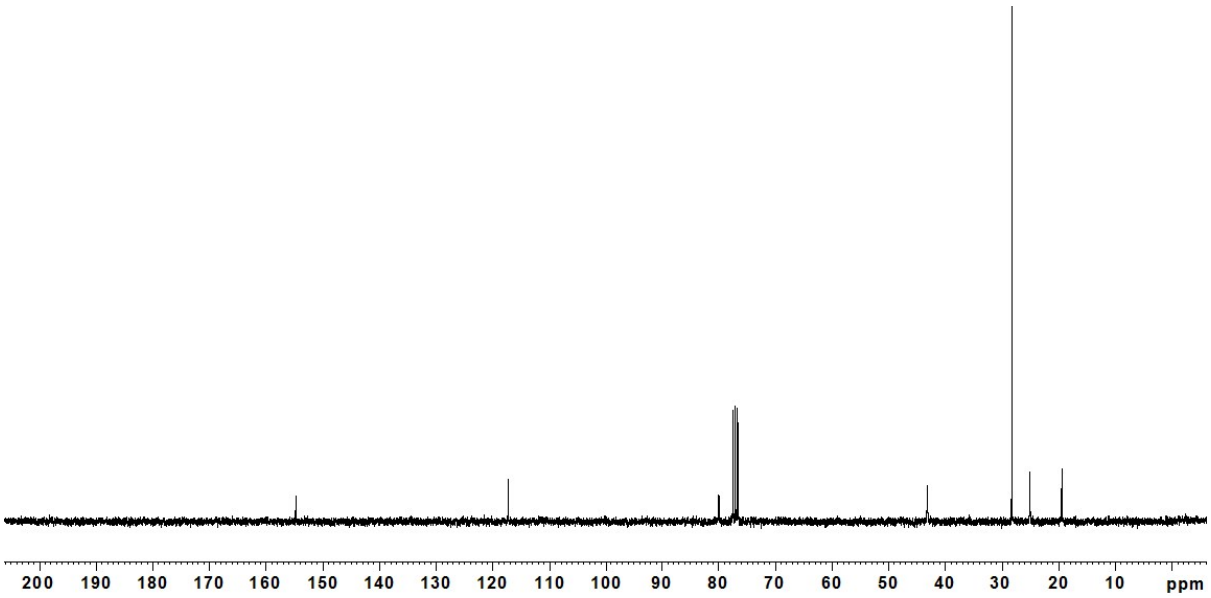


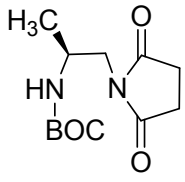

9.5
9.0
8.5
8.0
7.5
7.0
6.5


H3C
HN
CN
BOC

(S)-15

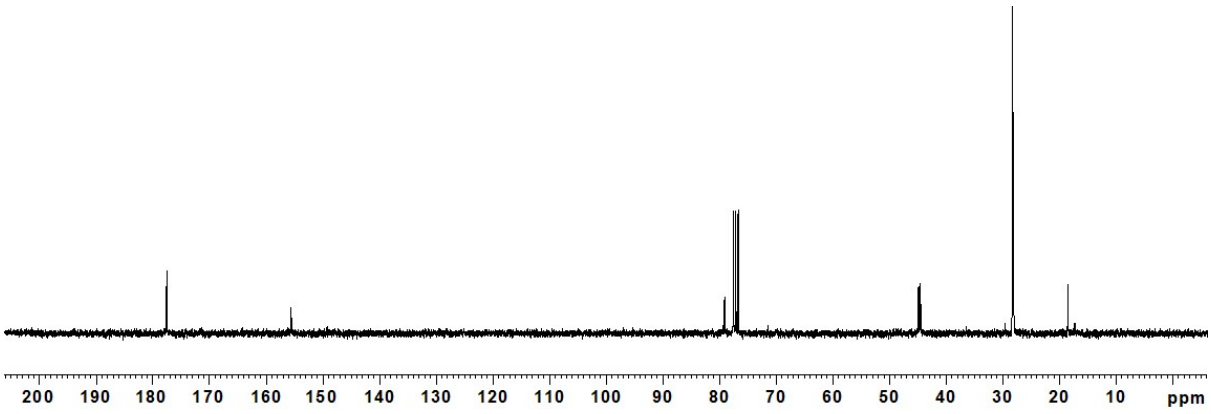

3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

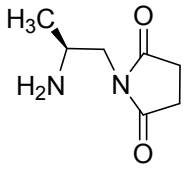

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


H3C
O
HN
N
BOC
O

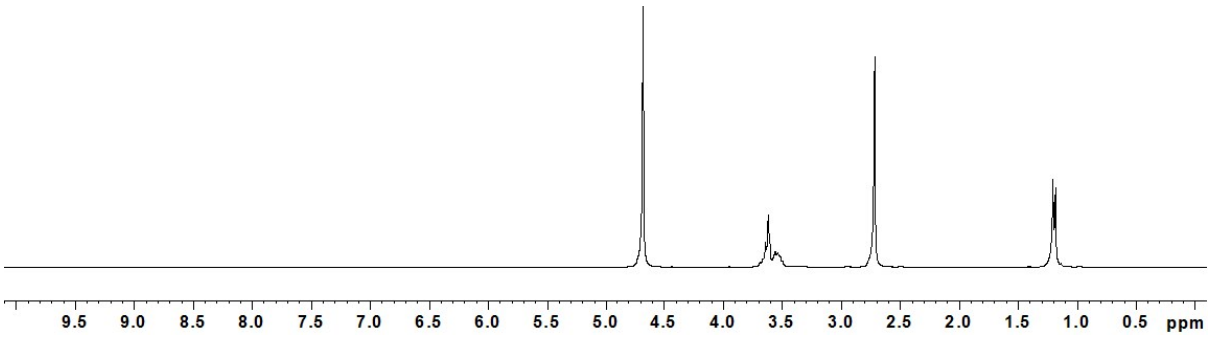
(S)-16

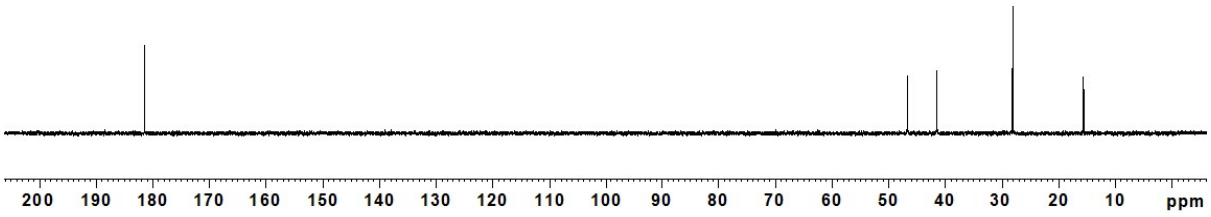
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

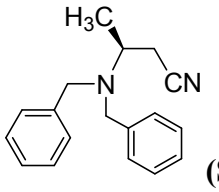

H3C
O
H2N
N
O

(S)-17


9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

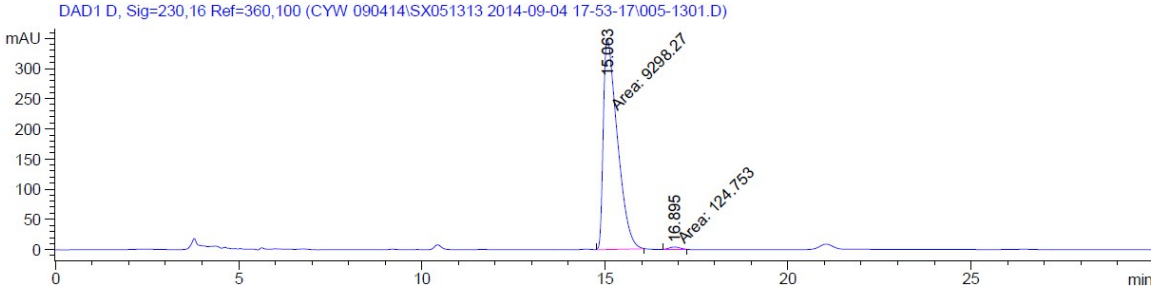
Chiral HPLC Chromatograms of Compounds



(S)-9aa

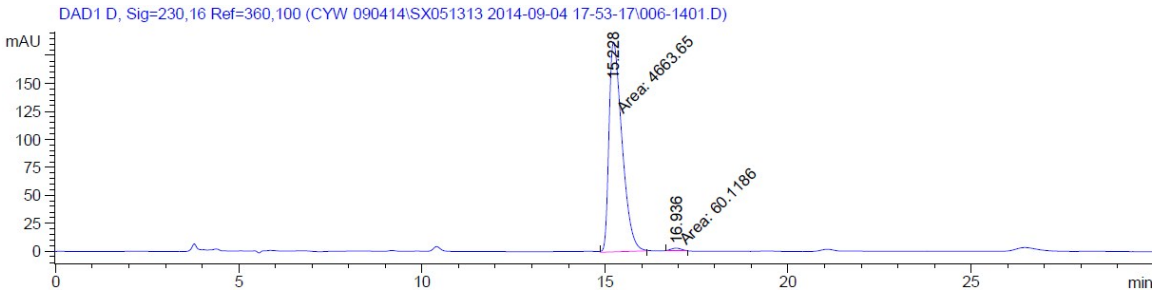
HPLC method A (1/99 = *i*-PrOH/Hexanes at a flow rate of 0.5 mL/min, 30 min)

Table 2, entry 1, solvent: CH_3CN, 97.4% e.e



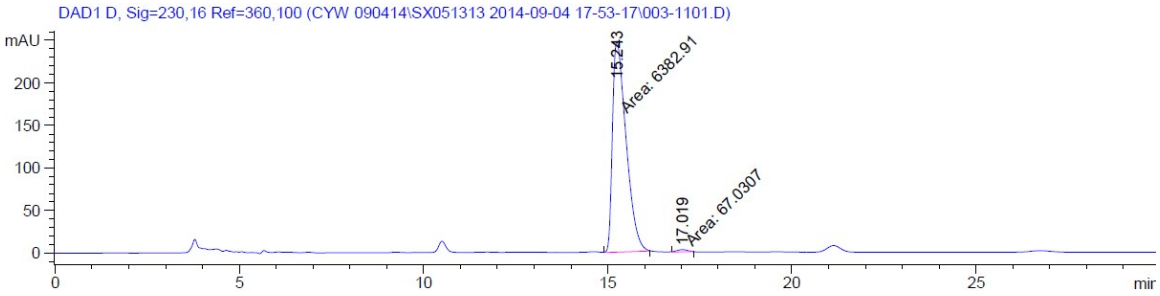
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.063	MM	0.4441	9298.27344	348.92560	98.6761
2	16.895	MM	0.4084	124.75290	5.09075	1.3239

Table 2, entry 2, solvent: DMSO, 97.5% e.e



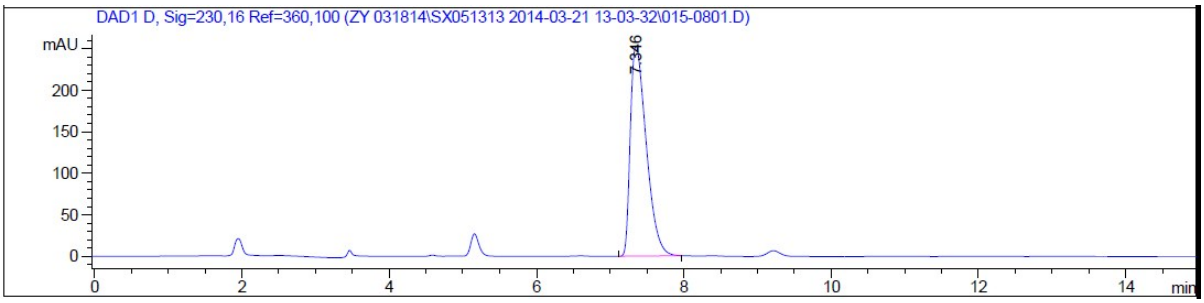
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.228	MM	0.4136	4663.65479	187.91025	98.7273
2	16.936	MM	0.3694	60.11864	2.71231	1.2727

Table 2, entry 3, solvent: CH_3CN/H_2O, 97.9% e.e



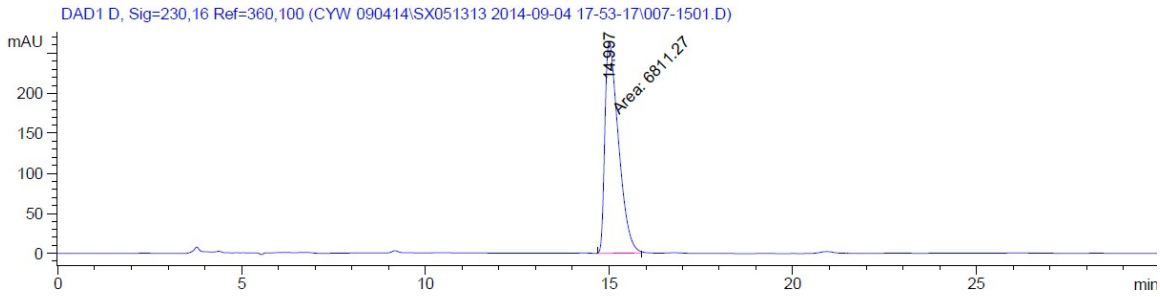
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.243	MM	0.4290	6382.91016	247.95433	98.9608
2	17.019	MM	0.3732	67.03071	2.99349	1.0392

Table 3, entry 1, >99% ee

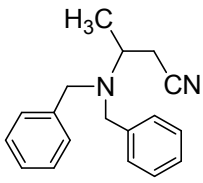


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.346	BB	0.2340	848.16101	56.23817	100.0000

Scheme 3, prepared as authentic sample, >99% ee

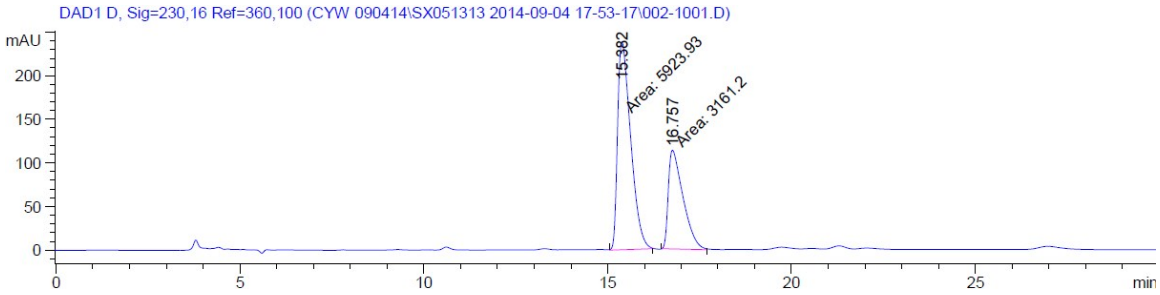


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.997	MM	0.4303	6811.27100	263.82727	100.0000

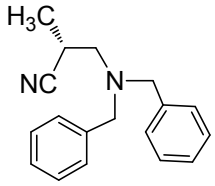


(rac)-9aa

HPLC method A (1/99 = *i*-PrOH/Hexanes at a flow rate of 0.5 mL/min, 30 min)



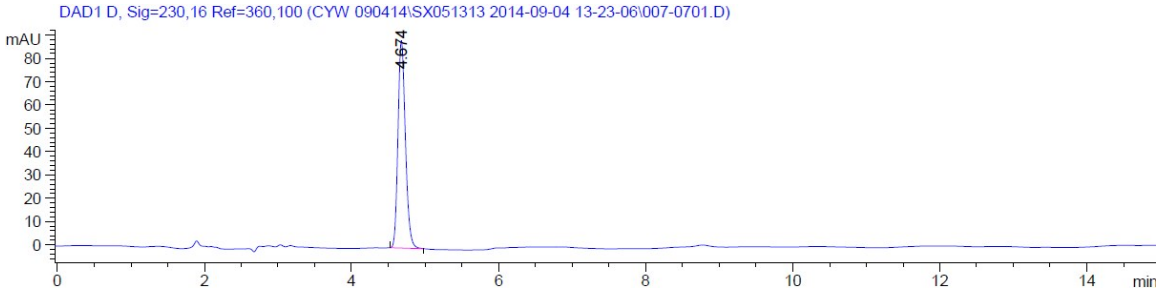
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.382	MM	0.4136	5923.92627	238.73009	65.2046
2	16.757	MM	0.4642	3161.20386	113.50059	34.7954



(R)-10aa

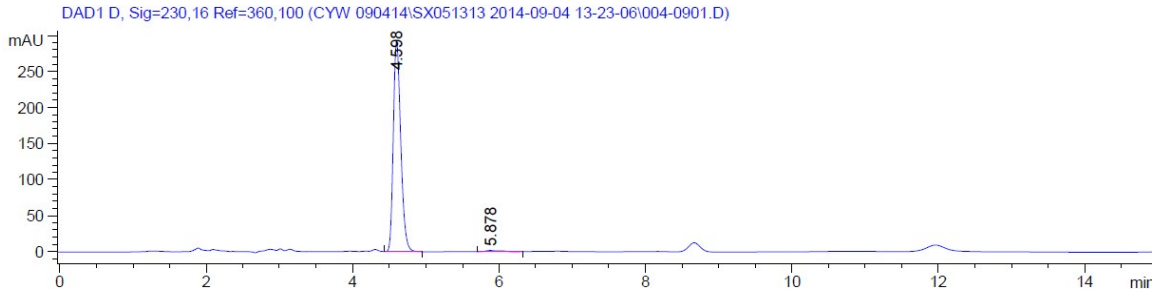
HPLC method B (1/99 = *i*-PrOH/Hexanes at a flow rate of 1 mL/min, 15 min)

Table 1, entry 1, solvent: CH_3CN, >99% e.e.



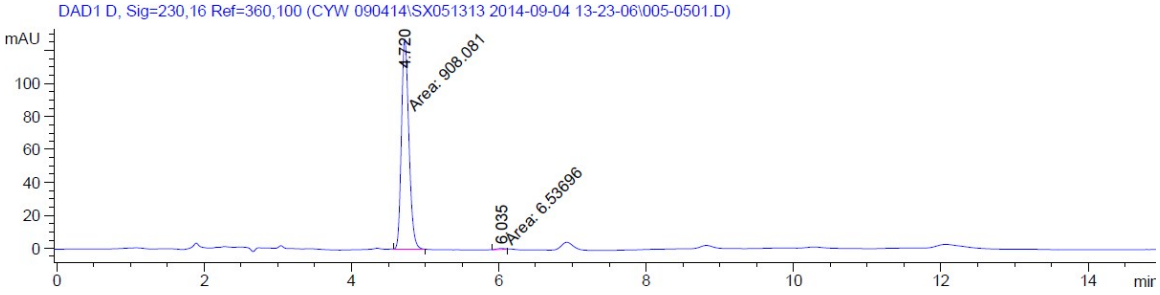
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.674	BB	0.1083	630.20349	89.33986	100.0000

Table 1, entry 2, solvent: DMSO, 97.9% e.e.

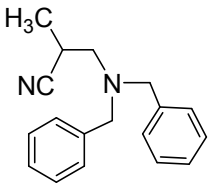


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.598	VB	0.1106	2070.28491	292.44000	98.9429
2	5.878	BB	0.1820	22.11900	1.69778	1.0571

Table 1, entry 3, solvent: CH_3CN/H_2O, 98.6% e.e.

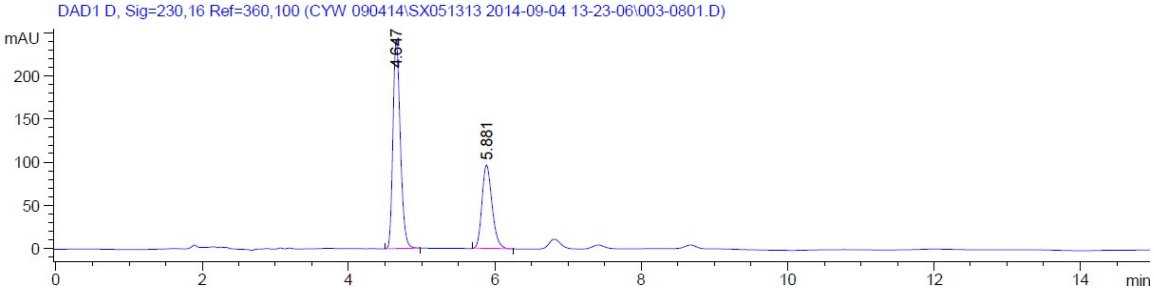


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.720	MM	0.1182	908.08057	128.04002	99.2853
2	6.035	MM	0.1487	6.53696	7.32456e-1	0.7147

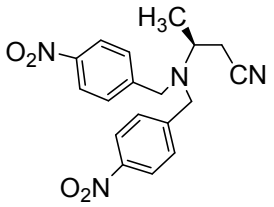


(rac)-10aa

HPLC method B (1/99 = *i*-PrOH/Hexanes at a flow rate of 1 mL/min, 15 min)



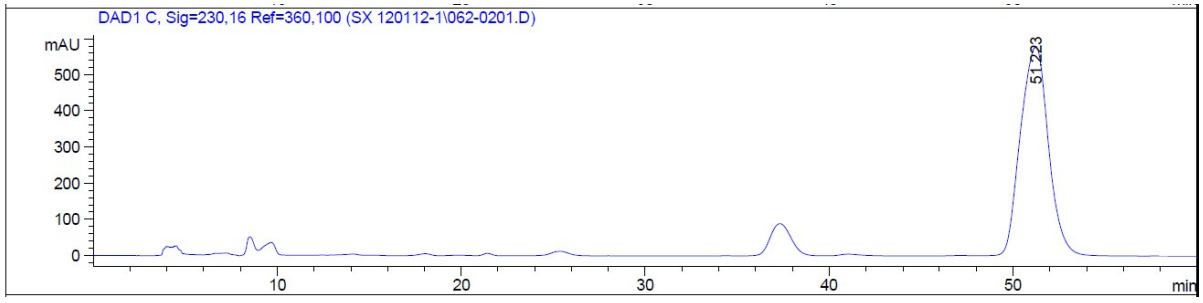
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.647	BB	0.1079	1704.35278	242.72006	64.6795
2	5.881	BB	0.1500	930.72015	96.95947	35.3205



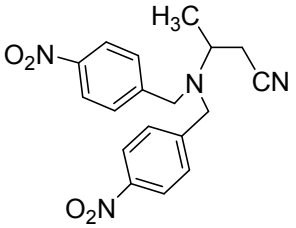
(S)-9b

Method C (8/92 = *i*-PrOH/Hexanes at a flow rate of 0.5 mL/min, 160 min)

Table 2, entry 4, >99% ee

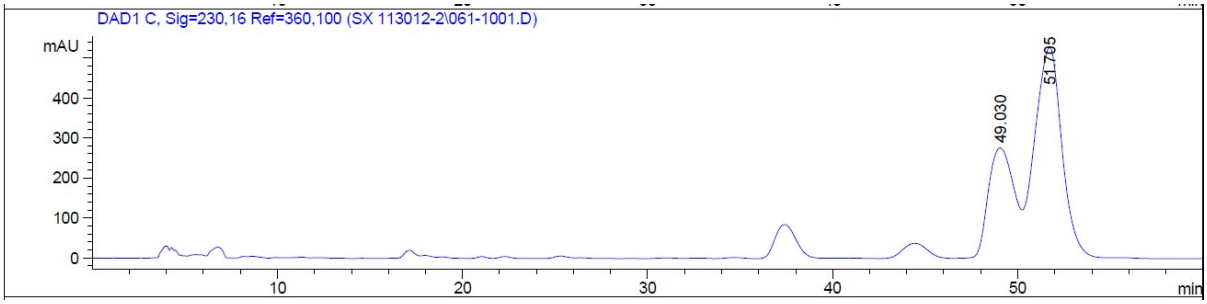


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	51.223	BB	1.4255	6.06854e4	578.66016	100.0000

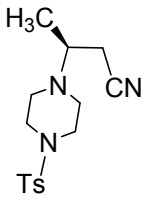


(rac)-9b

Method C (8/92 = *i*-PrOH/Hexanes at a flow rate of 0.5 mL/min, 160 min);



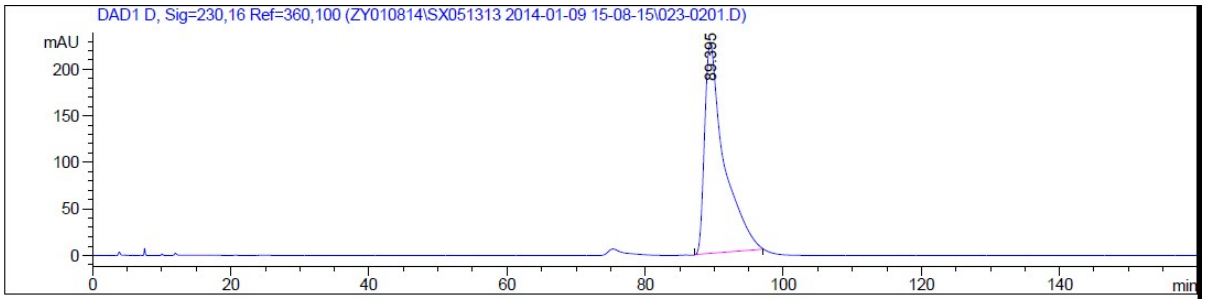
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	49.030	BV	1.4559	2.63756e4	275.27292	32.9264
2	51.705	VB	1.4573	5.37291e4	526.18042	67.0736



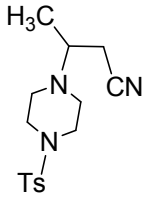
(S)-9c

Method D (8/92 = *i*-PrOH/Hexanes at a flow rate of 0.5 mL/min, 160 min);

Table 2, entry 5, >99% ee

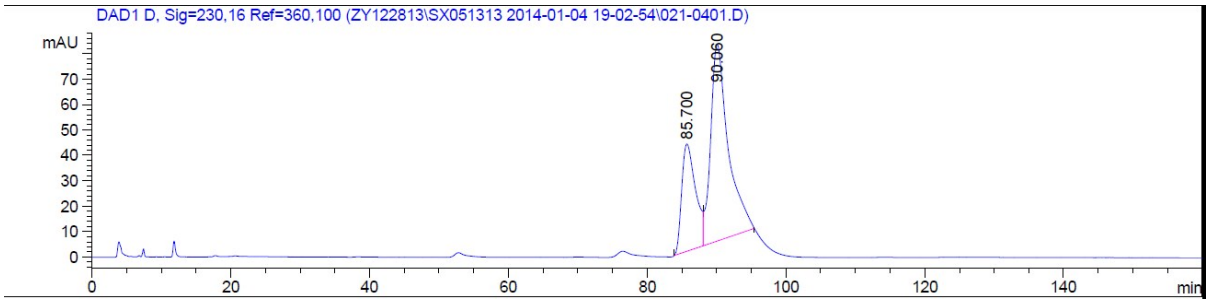


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	66.082	BB	1.7125	1.03662e4	85.62219	100.0000

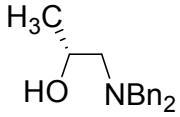


(rac)-9c

Method D (8/92 = *i*-PrOH/Hexanes at a flow rate of 0.5 mL/min, 160 min)



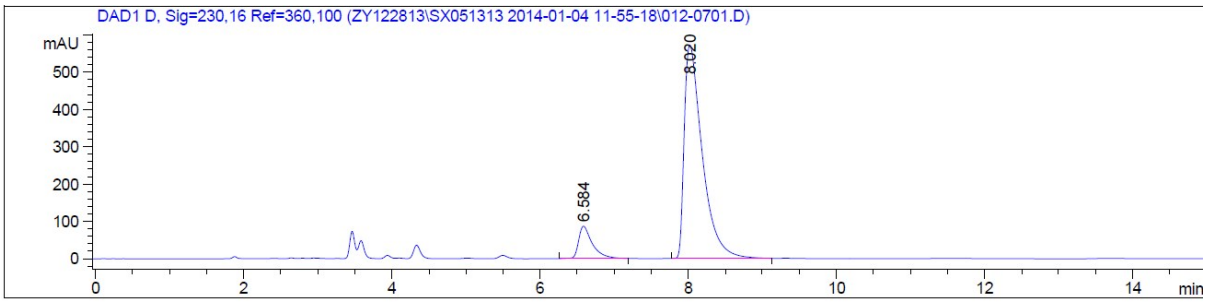
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	85.700	BV	1.8465	5863.63086	42.26819	29.9085
2	90.060	VB	2.3624	1.37416e4	77.58418	70.0915



(R)-9af

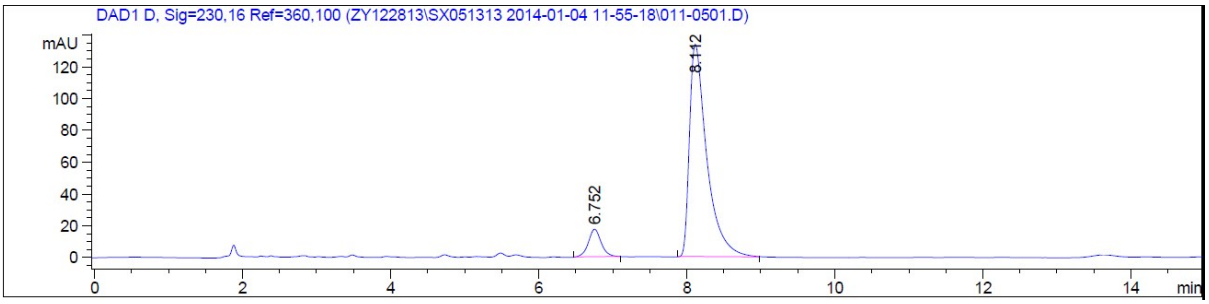
Method E (0.2/99.8 = *i*-PrOH/Hexanes at a flow rate of 0.5 mL/min, 15 min)

Table 3, entry 2, nucleophilic reagent: AgCN/H_2O, 79.5% ee.

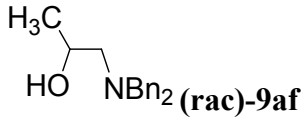


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.584	BB	0.1914	1130.74194	87.14746	10.4557
2	8.020	BB	0.2532	9683.87598	572.87152	89.5443

Table 3, from nitrate hydrolysis of (R)-15, 80.9% ee

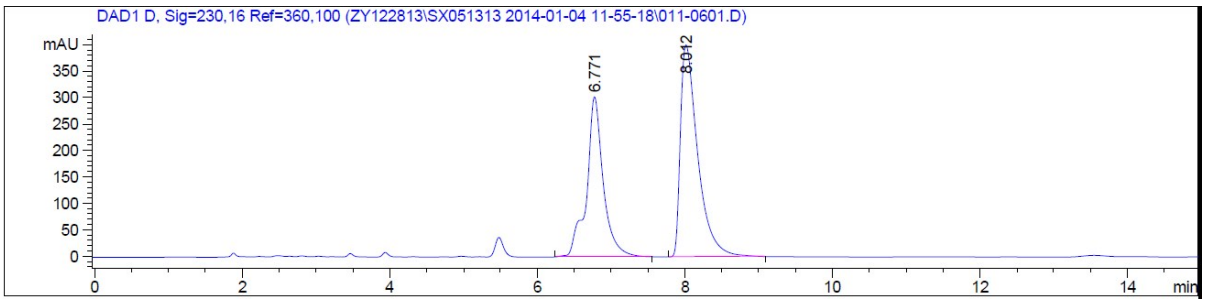


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.752	BB	0.1849	214.78168	17.53238	8.9569
2	8.112	BB	0.2403	2183.17725	133.87065	91.0431

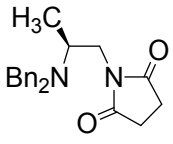


(rac)-9af

Method E (0.2/99.8 = *i*-PrOH/Hexanes at a flow rate of 0.5 mL/min, 15 min)



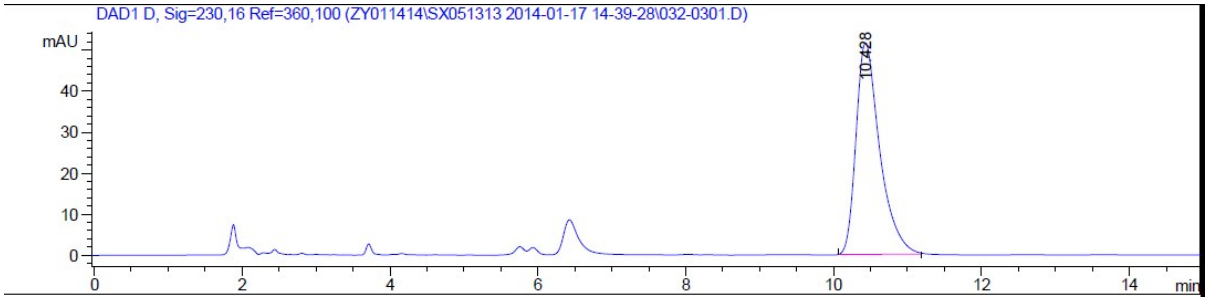
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.771	BB	0.2243	4782.09717	302.66464	42.2477
2	8.012	BB	0.2445	6537.09619	400.32202	57.7523



(S)-11

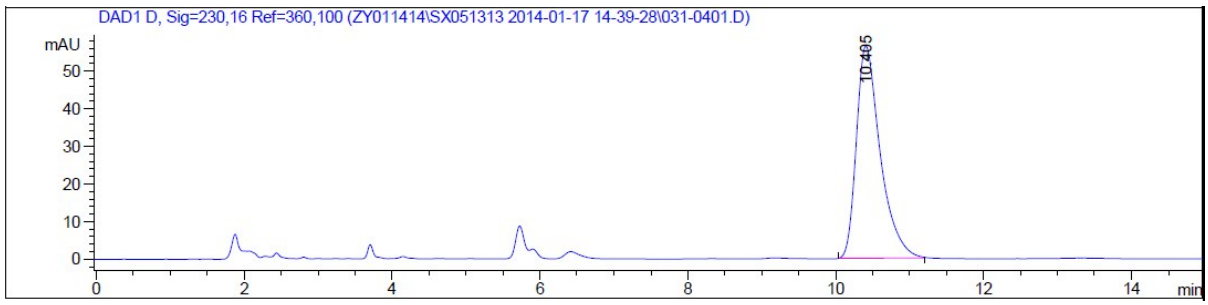
Method F (3/97 = *i*-PrOH/Hexanes at a flow rate of 1 mL/min, 15 min).

Table 3, entry 4, nucleophilic reagent: Ag_2CO_3, 99% ee.

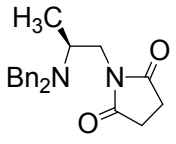


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.428	BB	0.3346	1153.77698	51.65539	100.0000

Table 3, entry 3, nucleophilic reagent: 1M NaOH, >99% ee.

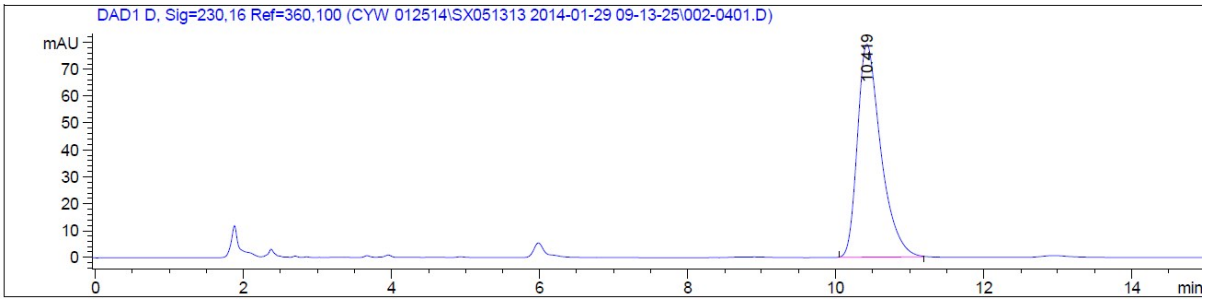


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.405	BB	0.3364	1271.11780	56.50495	100.0000

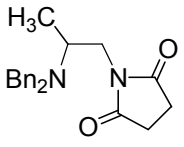


(S)-11

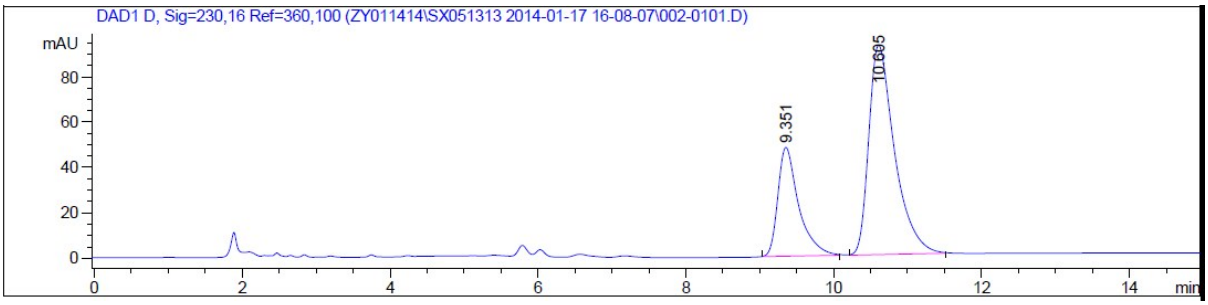
Scheme 3, prepared as authentic sample, >99% ee



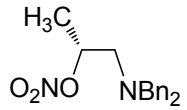
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.419	BB	0.3311	1745.52271	79.19775	100.0000



(rac)-11

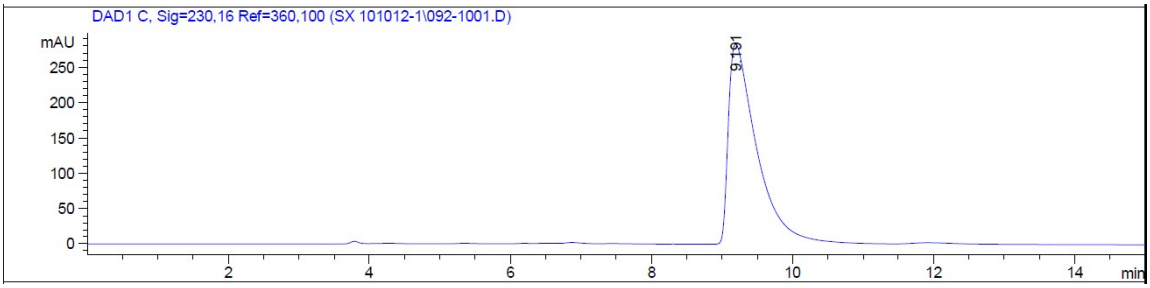


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.351	BB	0.2913	946.70941	48.17430	29.6655
2	10.605	BB	0.3631	2244.57373	92.50626	70.3345

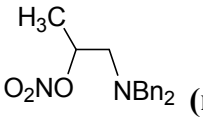


(R)-12

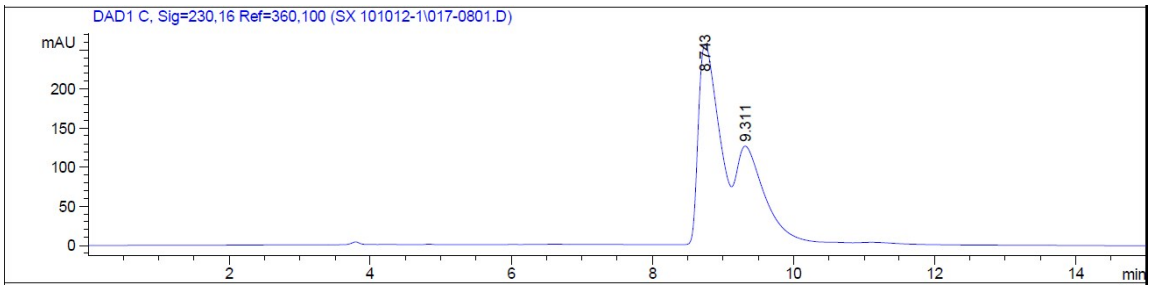
Table 3, entry 5, nucleophilic reagent: $AgNO_3/H_2O$, >99% ee.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.191	BB	0.4044	7880.58643	283.43564	100.0000



(rac)-12



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.743	BV	0.3125	5232.98193	256.03314	59.5829
2	9.311	VB	0.4163	3549.71289	124.61929	40.4171