

Supporting Information**Enantioselective Addition of Bromonitromethane to Aliphatic N-Boc Aldimines Using a Homogeneous Bifunctional Chiral Organocatalyst**

Kenneth E. Schwieter and Jeffrey N. Johnston*

Department of Chemistry and Vanderbilt Institute of Chemical Biology,
Vanderbilt University, Nashville, Tennessee 37235

Email: jeffrey.n.johnston@vanderbilt.edu

SI-II-X

Figure 1. ^1H NMR (400 MHz, CDCl_3) of 3p.....	3
Figure 2. ^{13}C NMR (100 MHz, CDCl_3) of 3p.....	4
Figure 3. ^1H NMR (400 MHz, CDCl_3) of 3r.....	5
Figure 4. ^{13}C NMR (100 MHz, CDCl_3) of 3r.....	6
Figure 5. ^1H NMR (400 MHz, CDCl_3) of <i>ent</i> -4b.....	7
Figure 6. ^{13}C NMR (100 MHz, CDCl_3) of <i>ent</i> -4b.....	8
Figure 7. ^1H NMR (400 MHz, CDCl_3) of <i>ent</i> -4p.....	9
Figure 8. ^{13}C NMR (100 MHz, CDCl_3) of <i>ent</i> -4p.....	10
Figure 9. ^1H NMR (400 MHz, CDCl_3) of <i>ent</i> -4r.....	11
Figure 10. ^{13}C NMR (100 MHz, CDCl_3) of <i>ent</i> -4r.....	12
Figure 11. ^1H NMR (600 MHz, CDCl_3) of 11.....	13
Figure 12. ^1H NMR (600 MHz, CDCl_3) of 12.....	14
Figure 13. ^1H NMR (600 MHz, CDCl_3) of 13.....	15
Figure 14. ^1H NMR (600 MHz, CDCl_3) of 14.....	16
Figure 15. ^1H NMR (600 MHz, CDCl_3) of 15.....	17
Figure 16. ^1H NMR (400 MHz, CDCl_3) of 17.....	18
Figure 17. ^1H NMR (400 MHz, CDCl_3) of 18.....	19
Figure 18. HPLC trace of <i>ent</i> -4a.....	20
Figure 19. HPLC trace of <i>ent</i> -4b.....	21
Figure 20. HPLC trace of <i>ent</i> -4c.....	22
Figure 21. HPLC trace of <i>ent</i> -4d.....	23
Figure 22. HPLC trace of <i>ent</i> -4e.....	24
Figure 23. HPLC trace of <i>ent</i> -4f.....	25
Figure 24. HPLC trace of <i>ent</i> -4g.....	26
Figure 25. HPLC trace of <i>ent</i> -4h.....	27
Figure 26. HPLC trace of <i>ent</i> -4i.....	28
Figure 27. HPLC trace of <i>ent</i> -4j.....	29
Figure 28. HPLC trace of <i>ent</i> -4k.....	30
Figure 29. HPLC trace of <i>ent</i> -4l.....	31
Figure 30. HPLC trace of <i>ent</i> -4m.....	32
Figure 31. HPLC trace of <i>ent</i> -4n.....	33
Figure 32. HPLC trace of <i>ent</i> -4o.....	34
Figure 33. HPLC trace of <i>ent</i> -4p.....	35
Figure 34. HPLC trace of <i>ent</i> -4q.....	36

Figure 35. HPLC trace of <i>ent</i> -4r	37
Figure 36. HPLC trace of <i>ent</i> -4s	38
Figure 37. HPLC trace of recrystallized 4a	39
Figure 38. HPLC trace of recrystallized 4e.	40
Figure 39. HPLC trace of recrystallized 4k.	41
Figure 40. HPLC trace of recrystallized 4m.	42
Figure 41. HPLC trace of recrystallized 4n.	43
Figure 42. HPLC trace of recrystallized 4o.	44
Figure 43. HPLC trace of recrystallized 4p.	45
References:	45

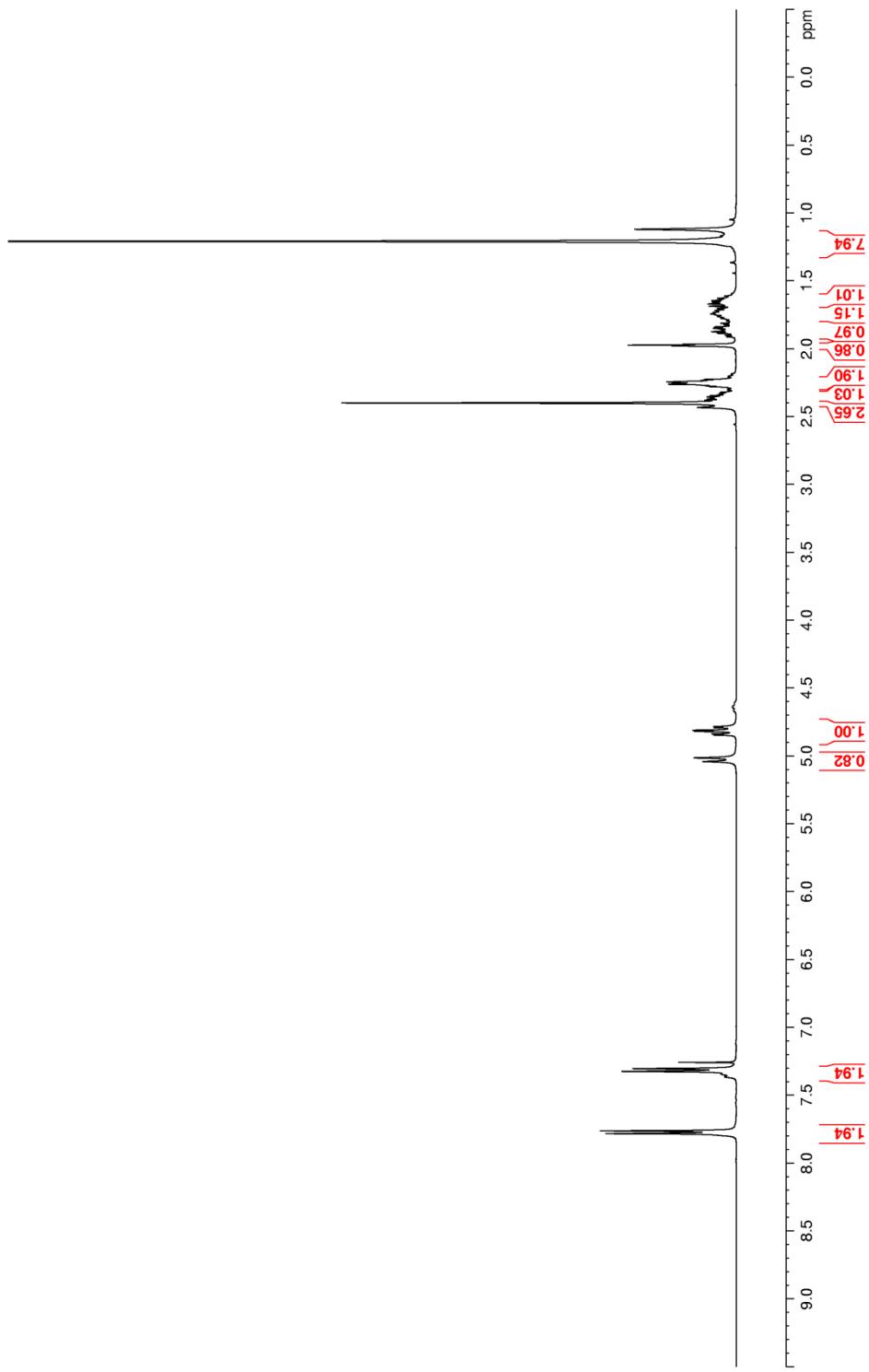
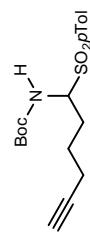
Figure 1. ^1H NMR (400 MHz, CDCl_3) of **3p**.

Figure 2. ^{13}C NMR (100 MHz, CDCl_3) of **3p**.

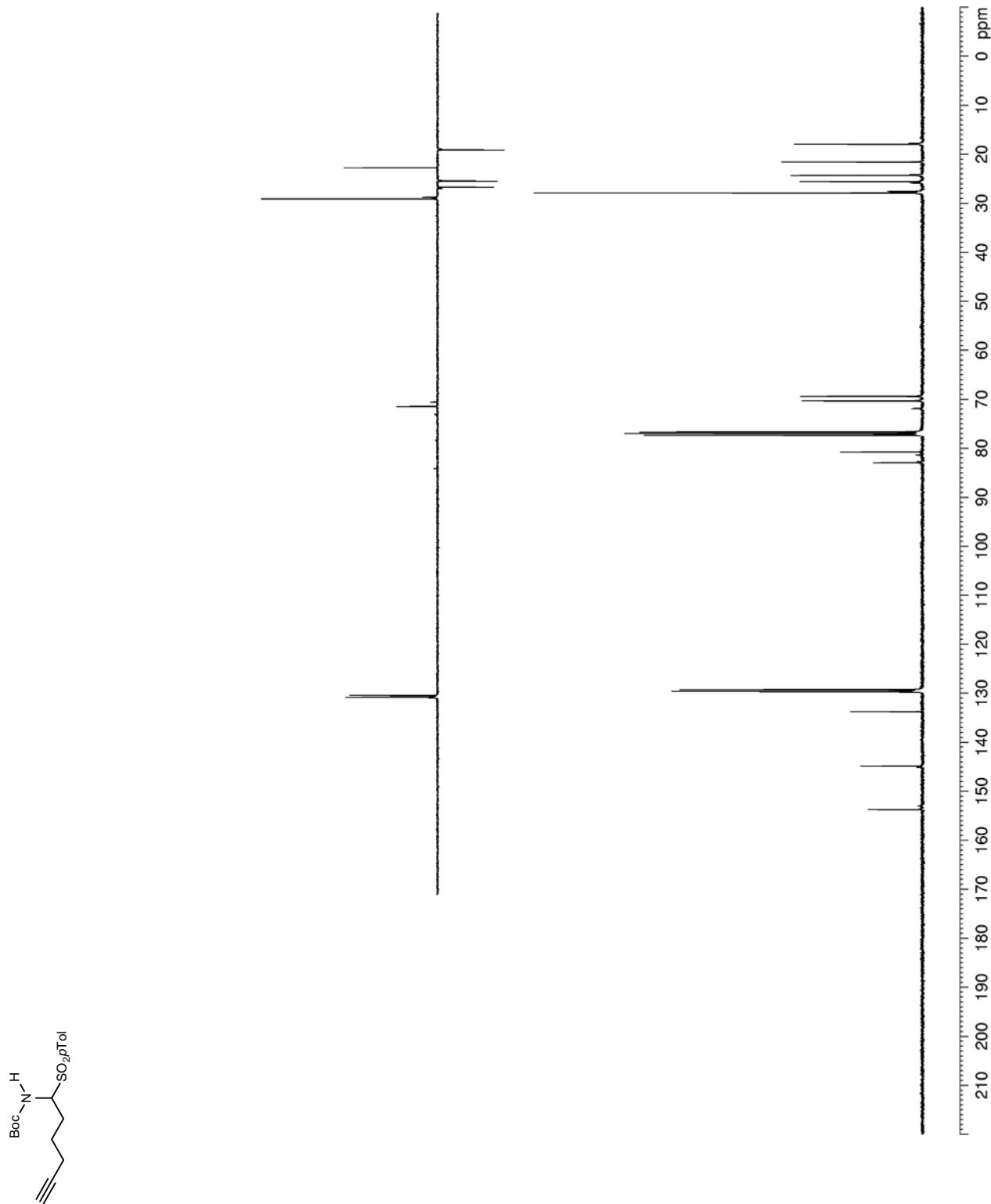


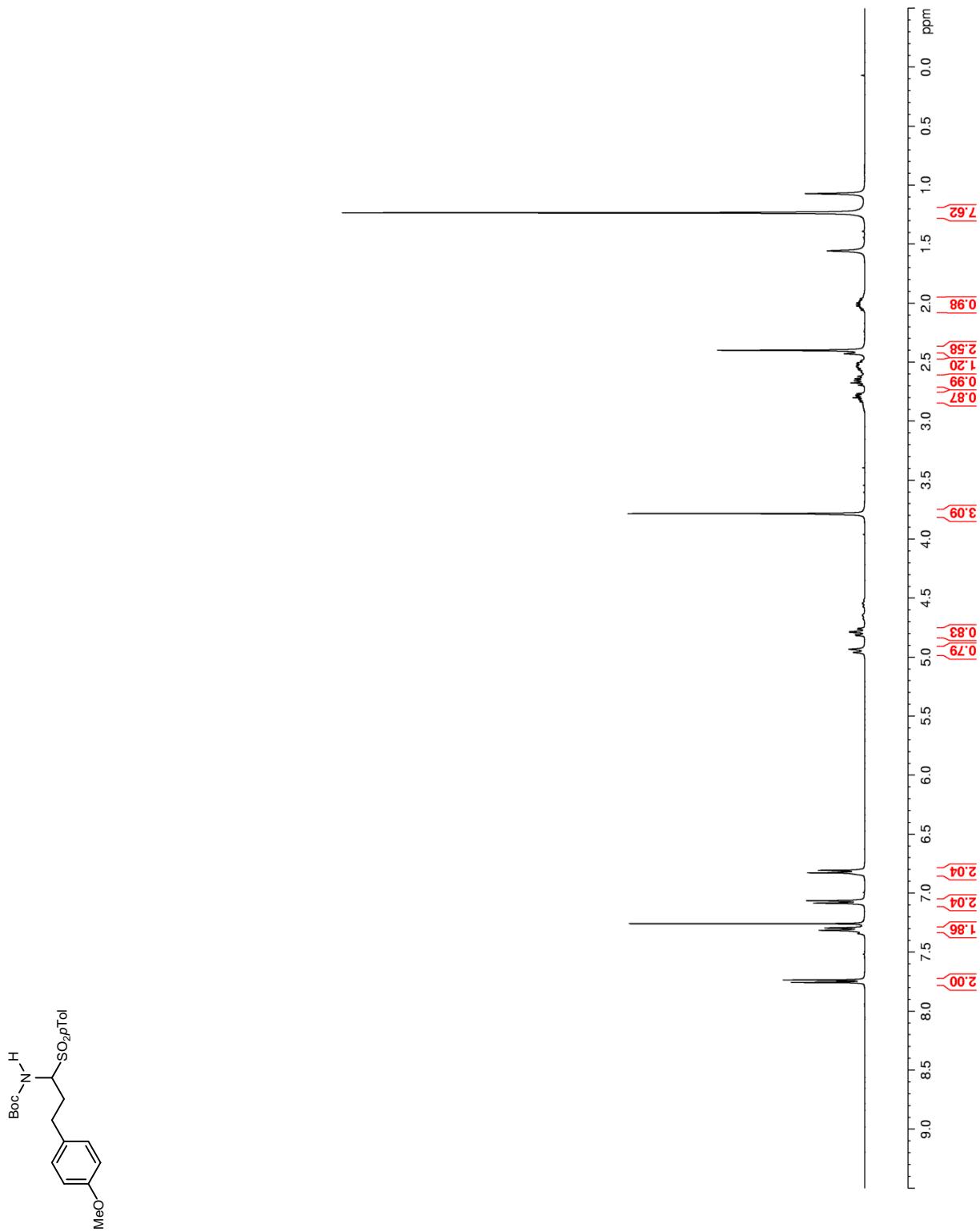
Figure 3. ^1H NMR (400 MHz, CDCl_3) of **3r**.

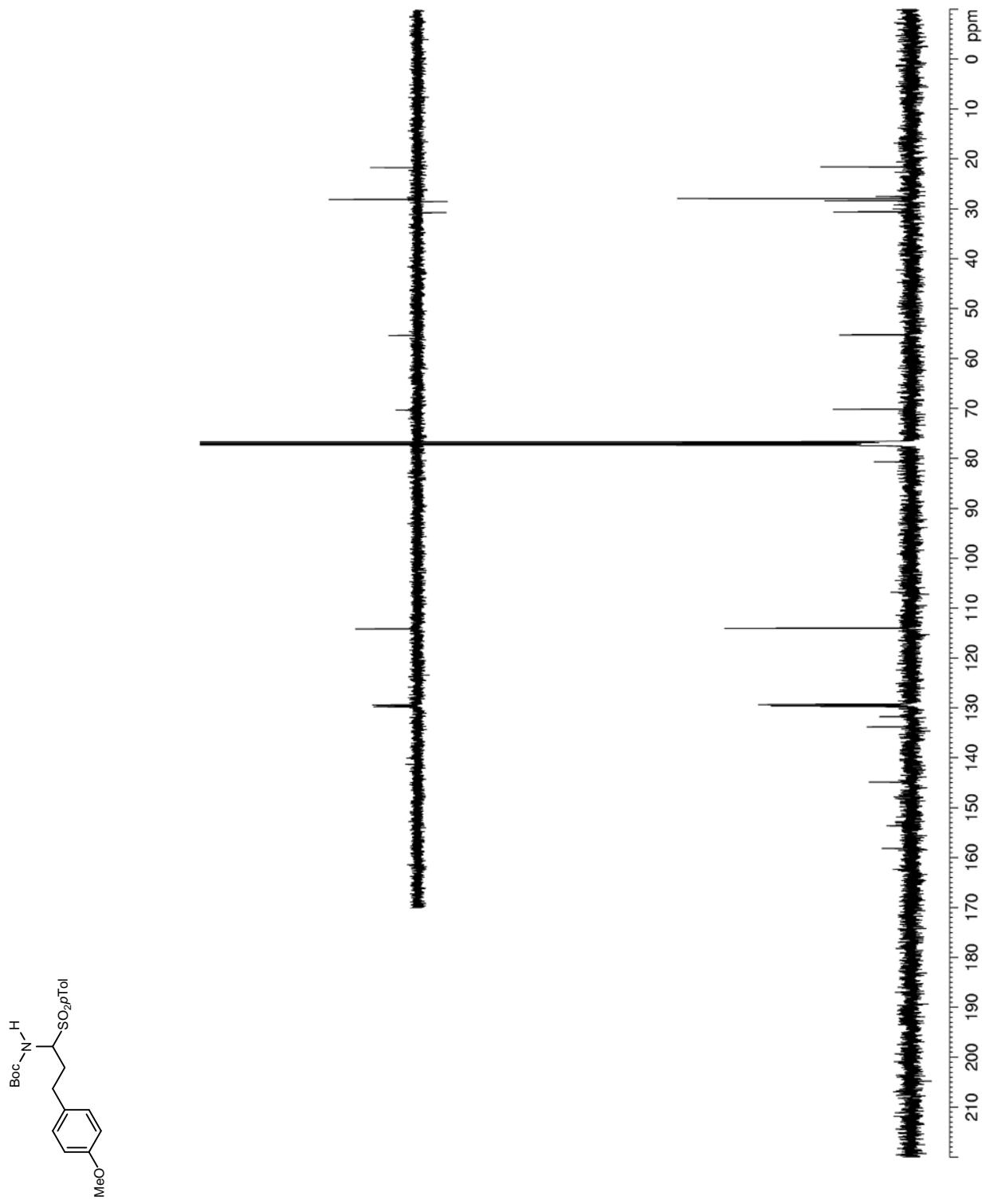
Figure 4. ^{13}C NMR (100 MHz, CDCl_3) of **3r**.

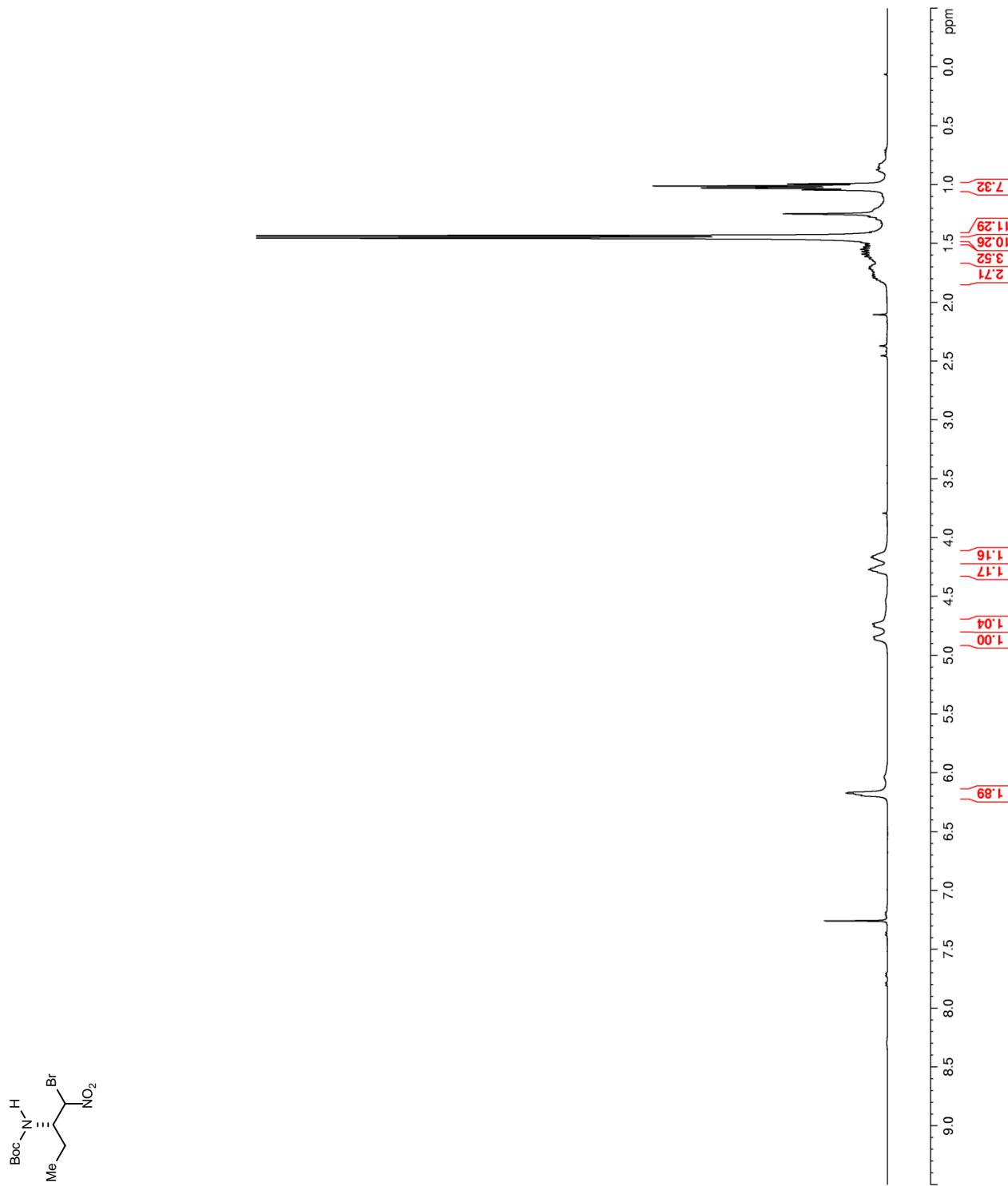
Figure 5. ^1H NMR (400 MHz, CDCl_3) of *ent*-4b.

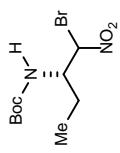
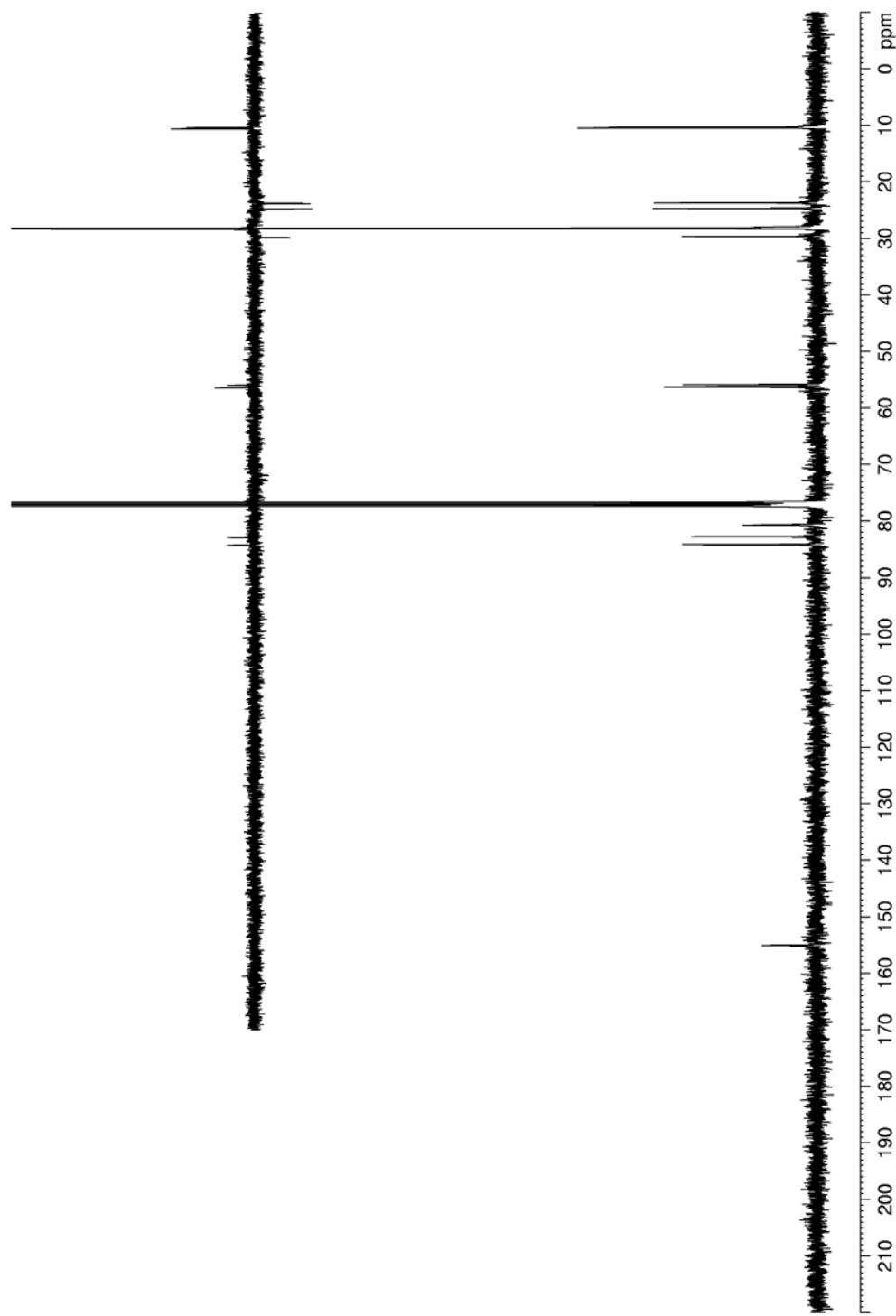
Figure 6. ^{13}C NMR (100 MHz, CDCl_3) of *ent*-4b.

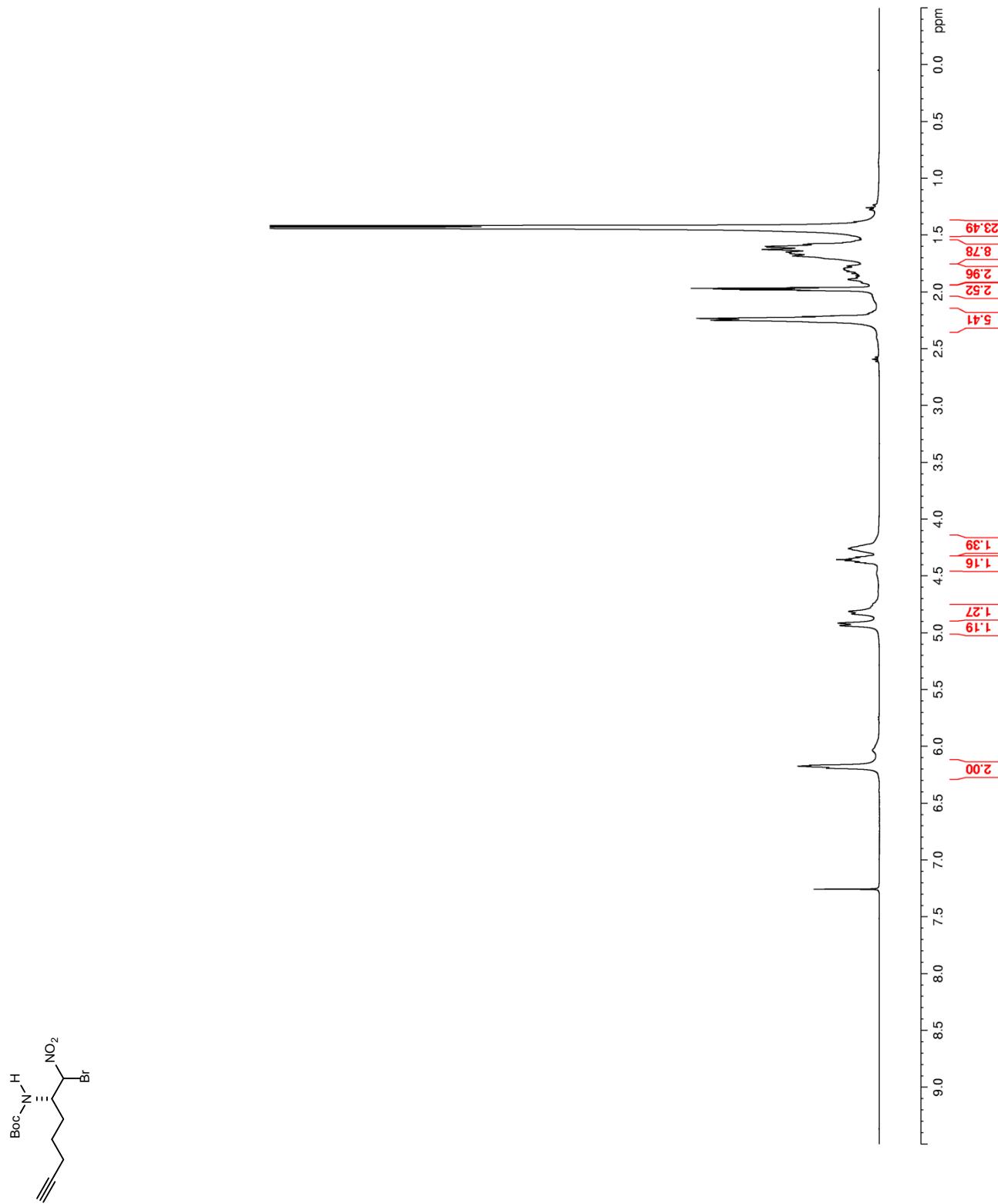
Figure 7. ^1H NMR (400 MHz, CDCl_3) of *ent*-4p.

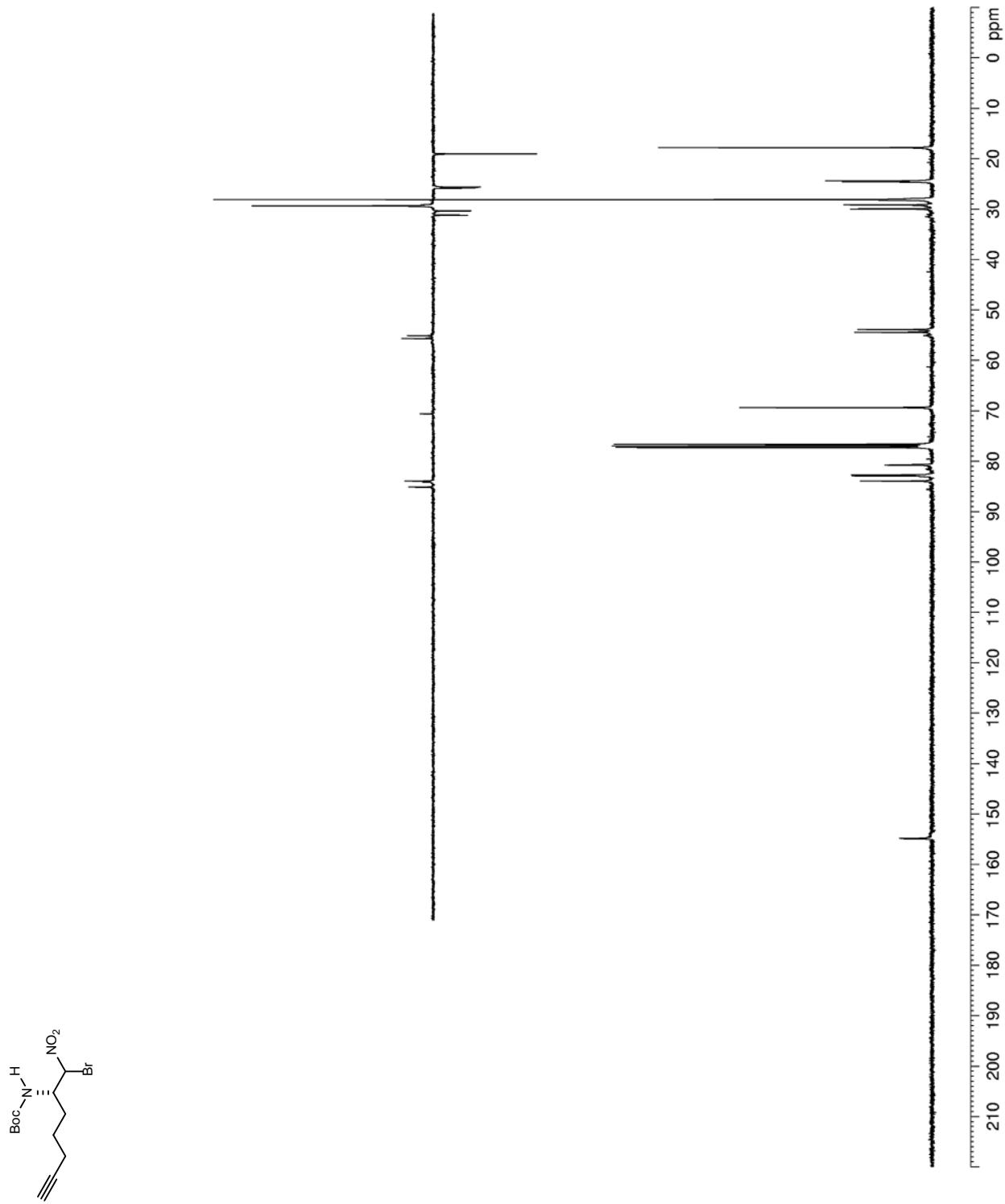
Figure 8. ^{13}C NMR (100 MHz, CDCl_3) of *ent*-4p.

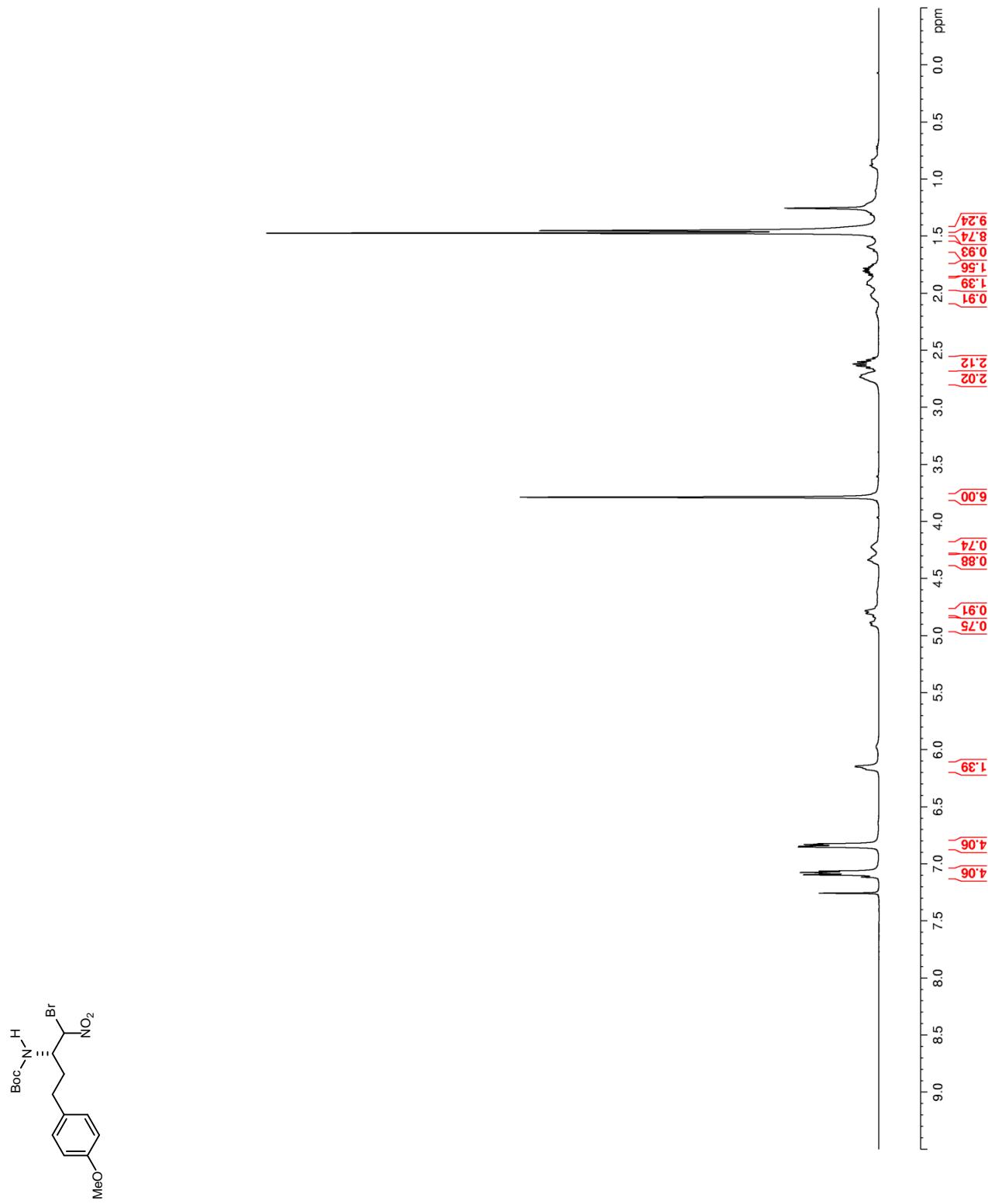
Figure 9. ^1H NMR (400 MHz, CDCl_3) of *ent*-4r.

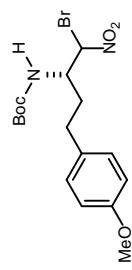
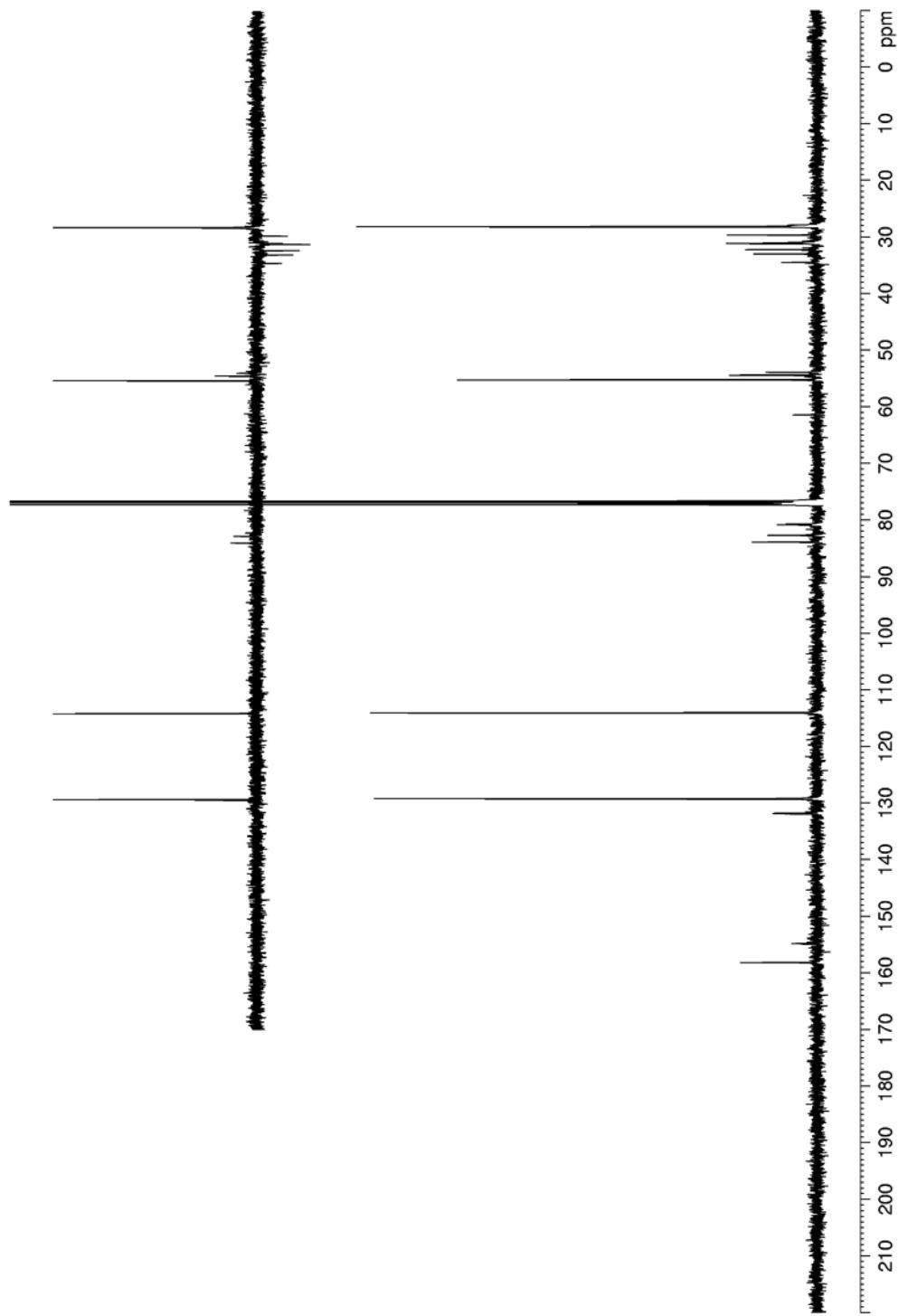
Figure 10. ^{13}C NMR (100 MHz, CDCl_3) of *ent*-4r.

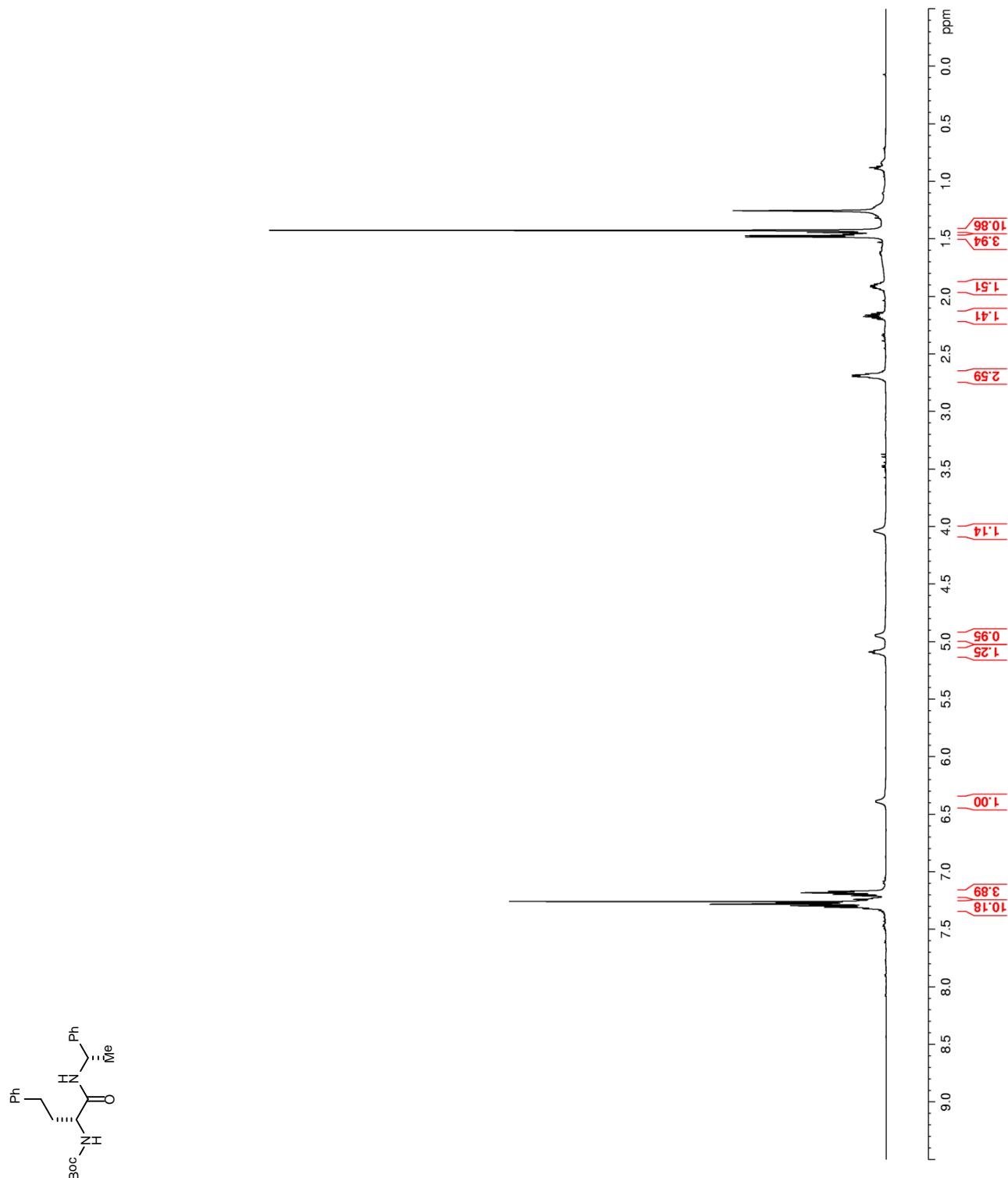
Figure 11. ^1H NMR (600 MHz, CDCl_3) of **11**.

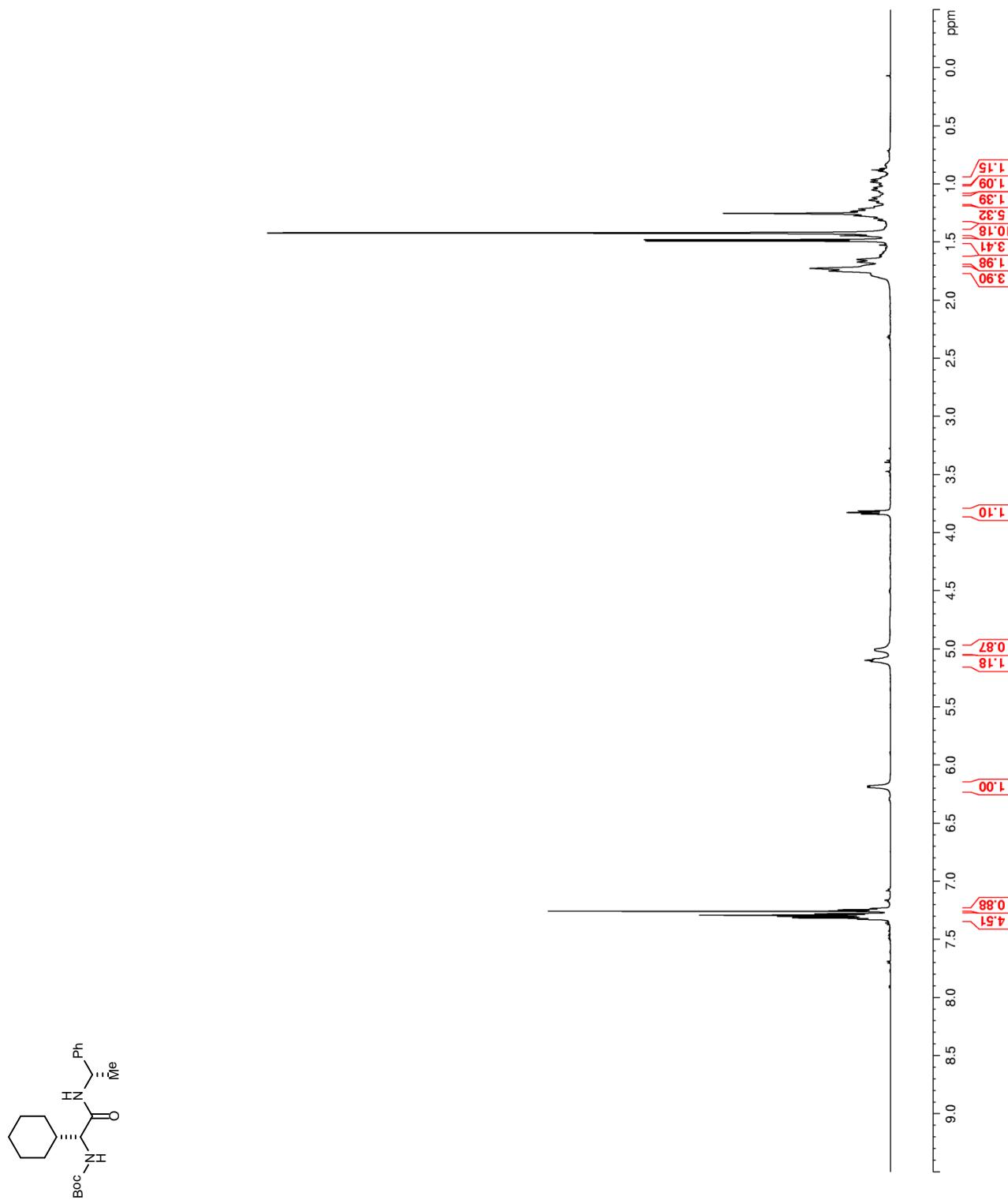
Figure 12. ^1H NMR (600 MHz, CDCl_3) of **12**.

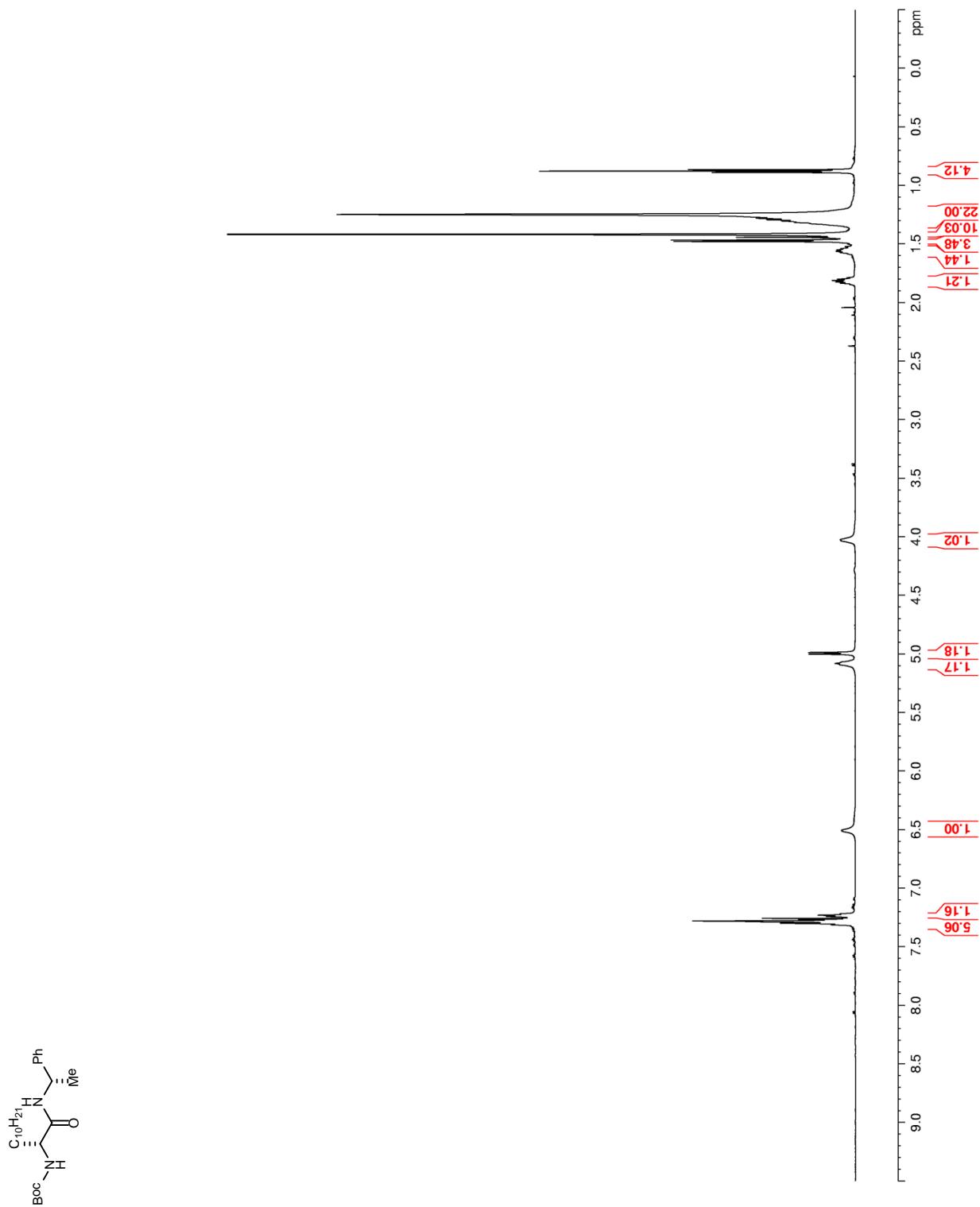
Figure 13. ^1H NMR (600 MHz, CDCl_3) of **13**.

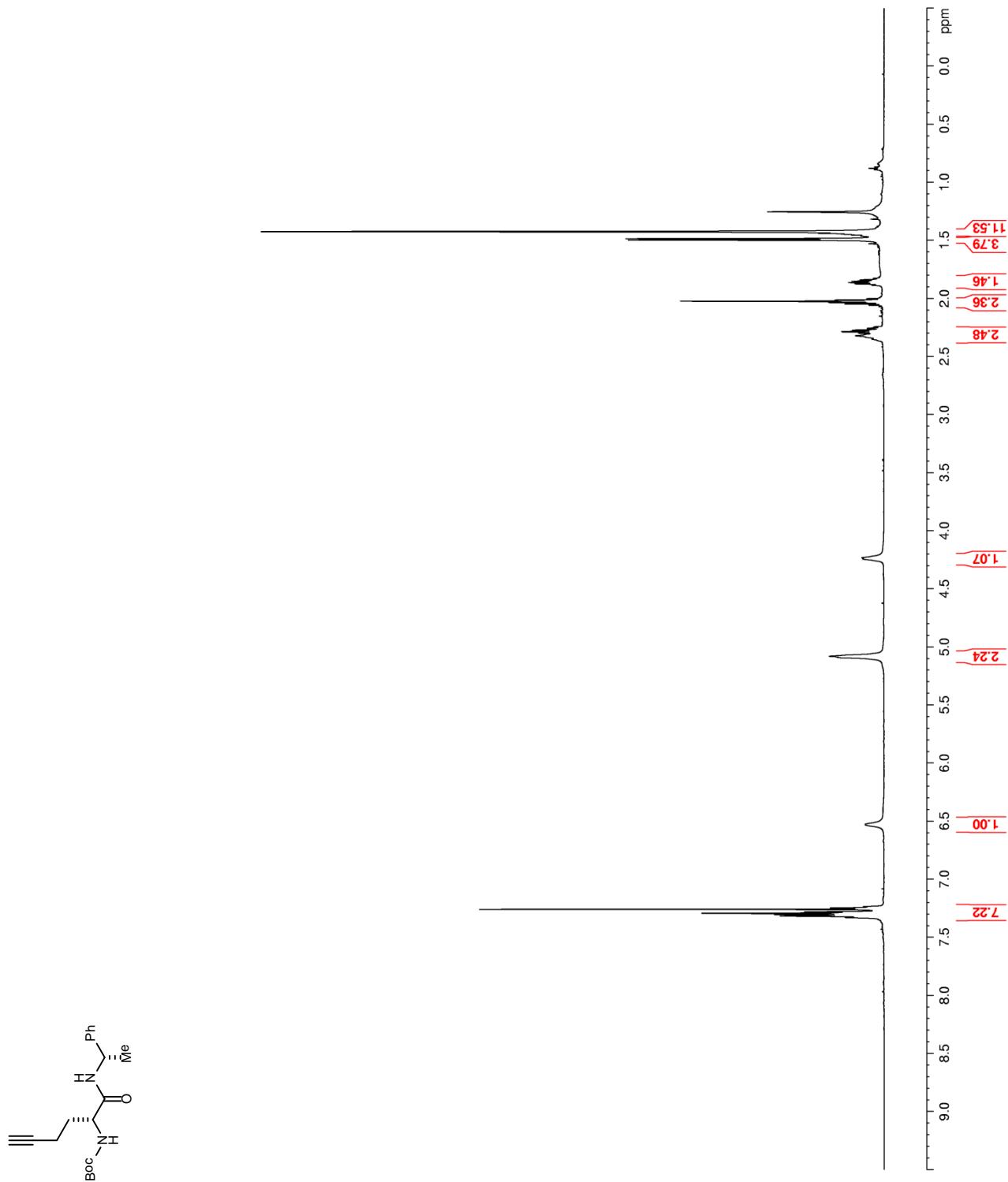
Figure 14. ^1H NMR (600 MHz, CDCl_3) of **14**.

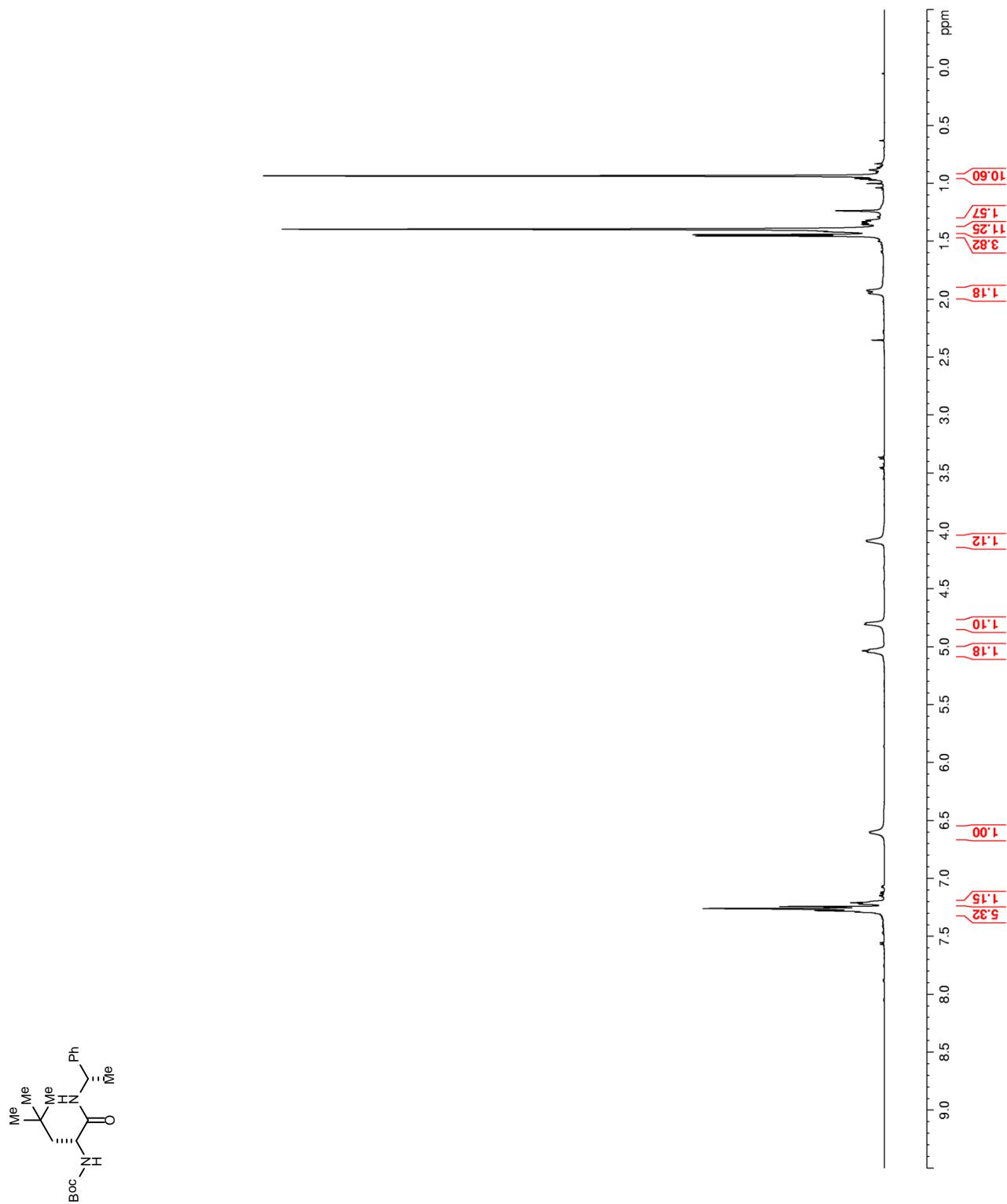
Figure 15. ^1H NMR (600 MHz, CDCl_3) of **15**.

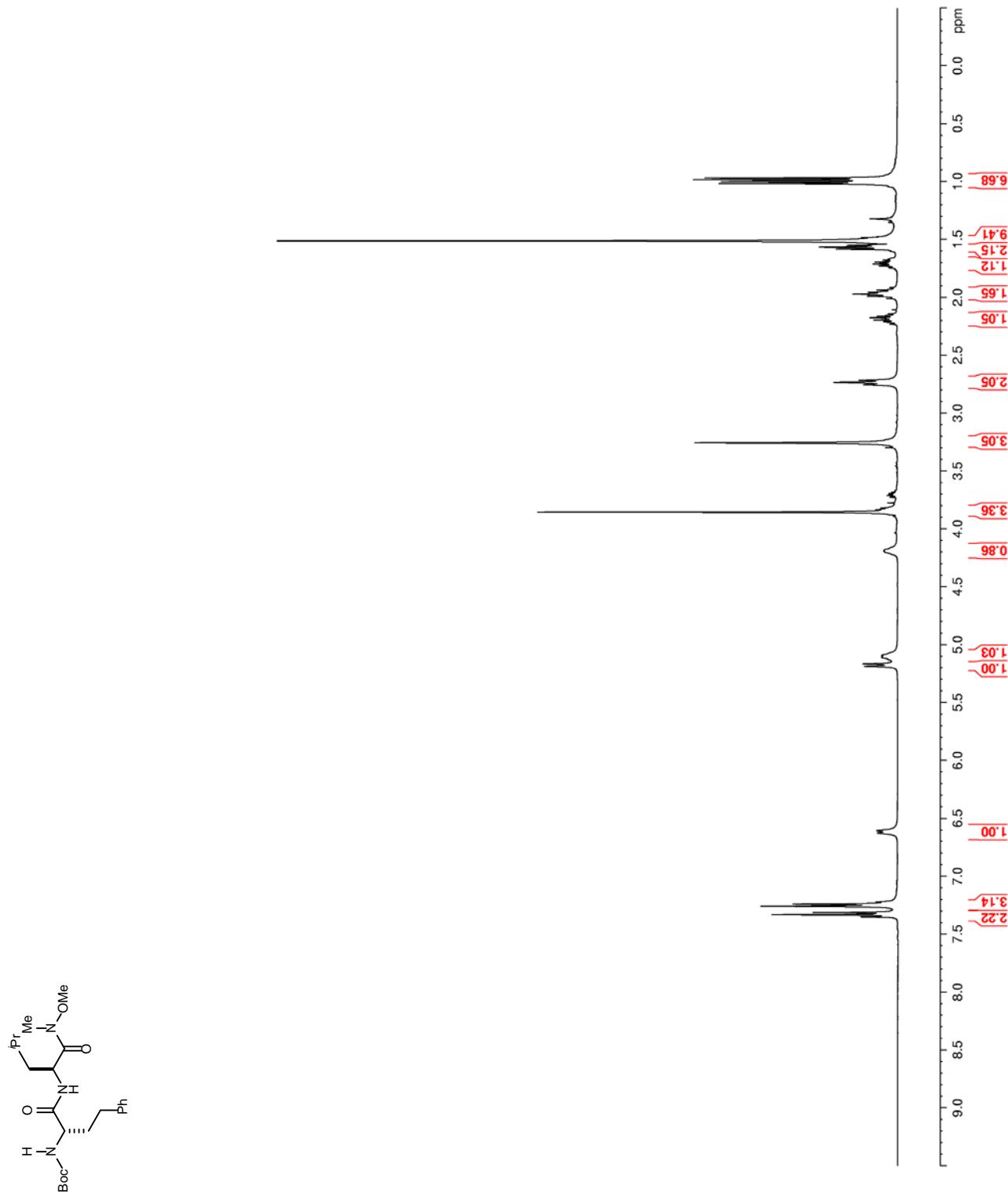
Figure 16. ^1H NMR (400 MHz, CDCl_3) of **17**.

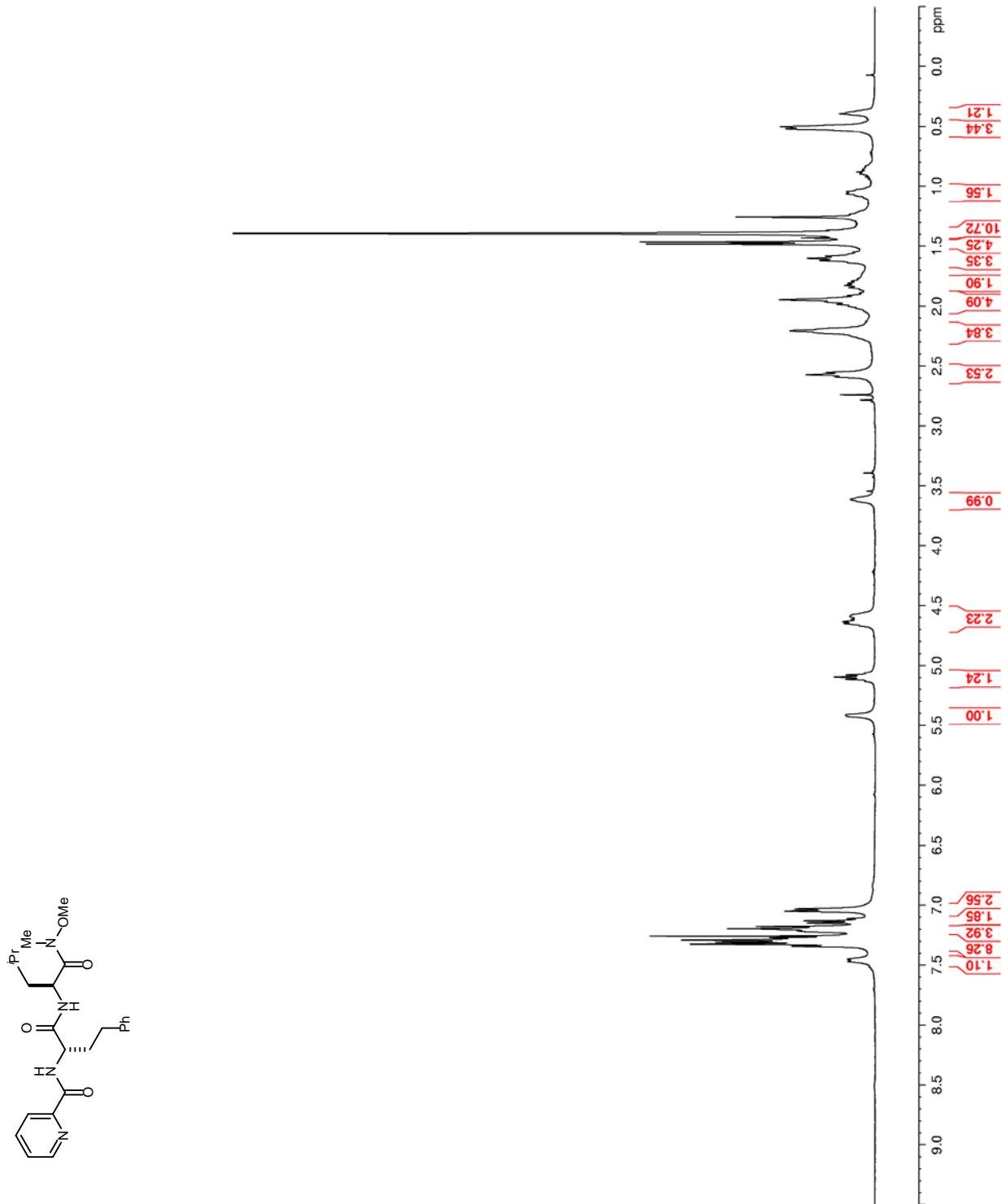
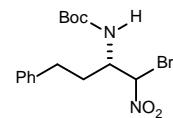
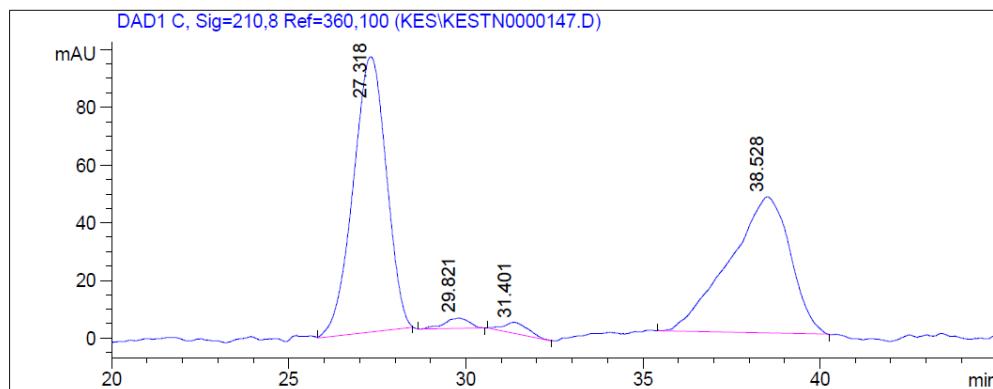
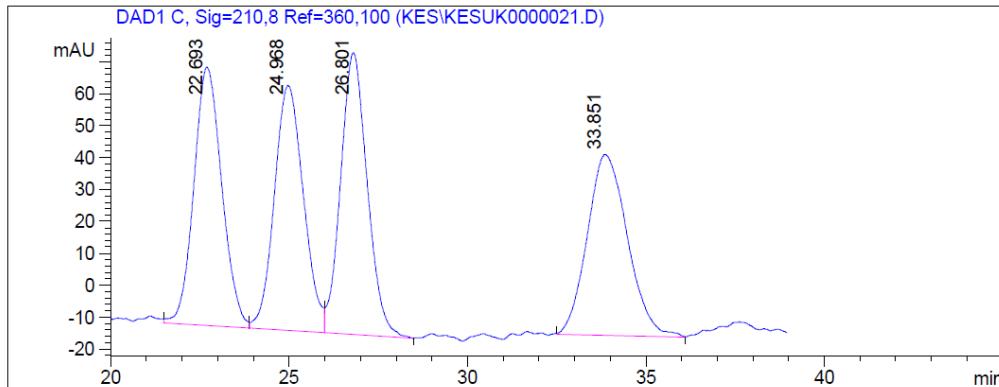
Figure 17. ^1H NMR (400 MHz, CDCl_3) of **18**.

Figure 18. HPLC trace of *ent*-4a.¹

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %

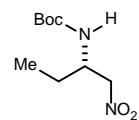
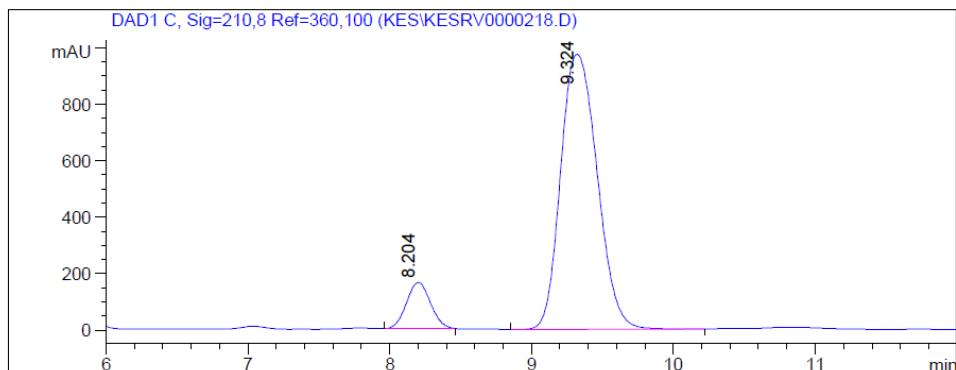
1	27.318	1.087	6228.133	50.88
2	29.821	0.814	177.088	1.45
3	31.401	0.819	189.864	1.55
4	38.528	1.995	5645.621	46.12



Signal 1: DAD1 C, Sig=210,8 Ref=360,100

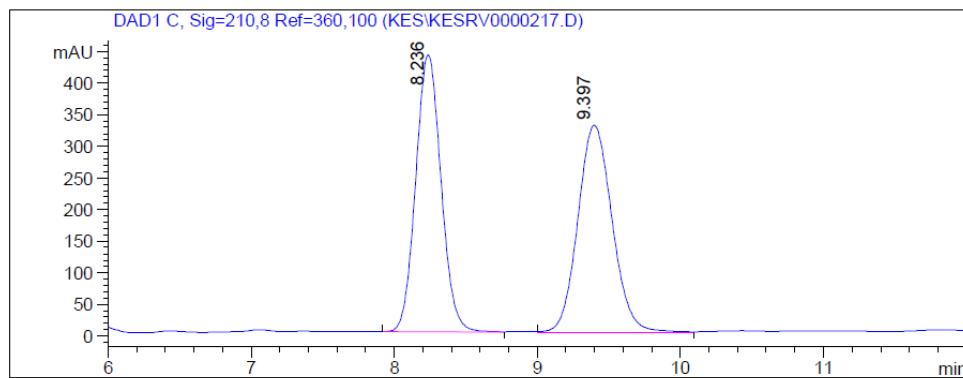
Peak #	RT [min]	Width [min]	Area	Area %

1	22.693	0.741	4426.310	24.85
2	24.968	0.734	4362.037	24.49
3	26.801	0.742	4577.324	25.70
4	33.851	0.952	4445.171	24.96

Figure 19. HPLC trace of *ent*-4b.

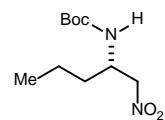
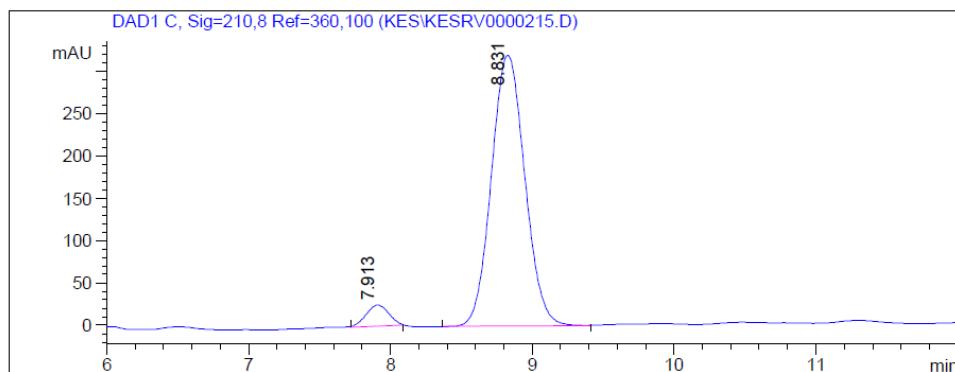
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	8.204	0.195	1905.083	9.79
2	9.324	0.300	17562.697	90.21



Signal 1: DAD1 C, Sig=210,8 Ref=360,100

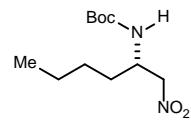
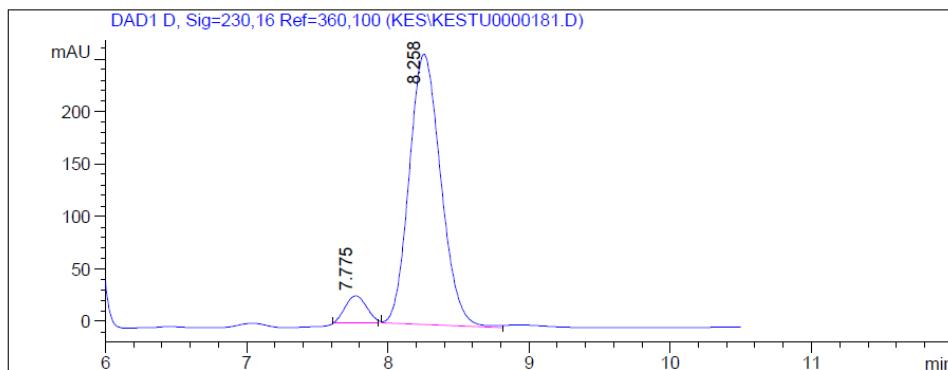
Peak #	RT [min]	Width [min]	Area	Area %
1	8.236	0.192	5398.217	49.91
2	9.397	0.257	5416.787	50.09

Figure 20. HPLC trace of *ent*-4c.

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

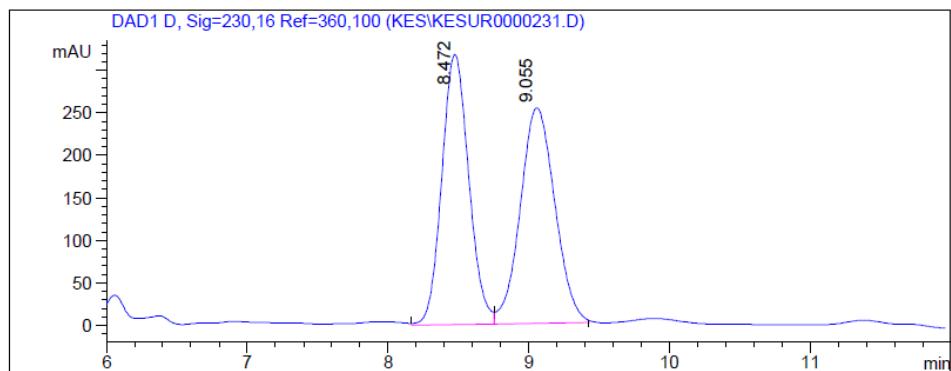
Peak #	RT [min]	Width [min]	Area	Area %
<hr/>				
1	7.913	0.186	278.133	5.03
2	8.831	0.274	5246.023	94.97

Based on literature assay.²

Figure 21. HPLC trace of *ent*-4d.

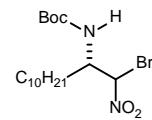
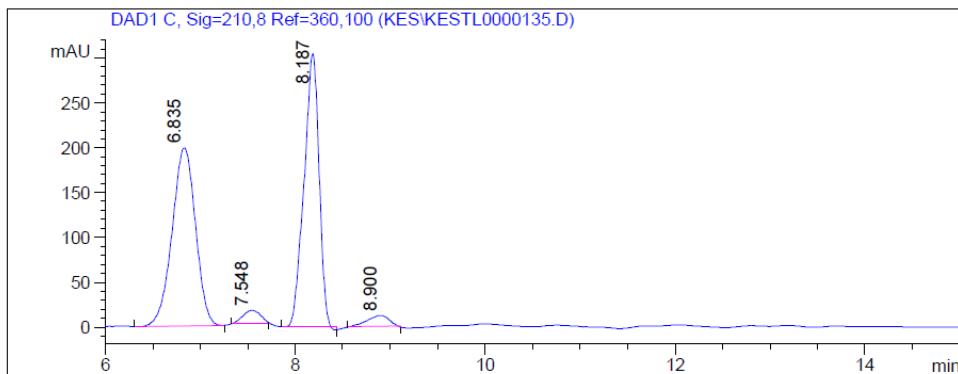
Signal 1: DAD1 D, Sig=230,16 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	7.775	0.173	266.171	6.26
2	8.258	0.258	3988.328	93.74



Signal 1: DAD1 D, Sig=230,16 Ref=360,100

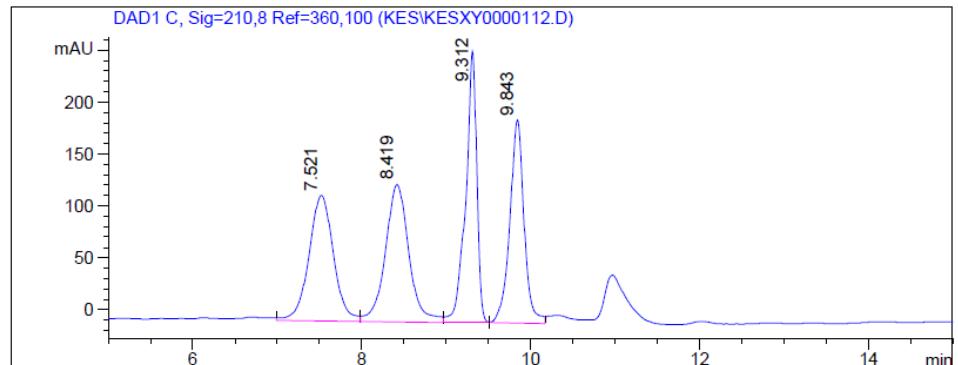
Peak #	RT [min]	Width [min]	Area	Area %
1	8.472	0.222	4244.789	49.50
2	9.055	0.284	4330.040	50.50

Figure 22. HPLC trace of *ent*-4e.

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %

1	6.835	0.286	3403.559	47.78
2	7.548	0.210	182.678	2.56
3	8.187	0.183	3347.163	46.99
4	8.900	0.264	189.731	2.66



Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %

1	7.521	0.309	2455.734	25.30
2	8.419	0.294	2563.828	26.41
3	9.312	0.131	2386.716	24.59
4	9.843	0.173	2300.407	23.70

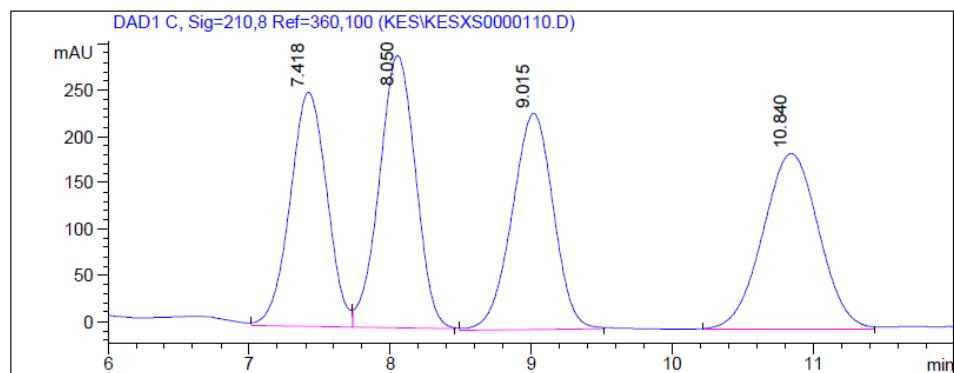
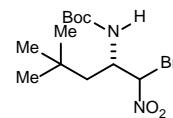
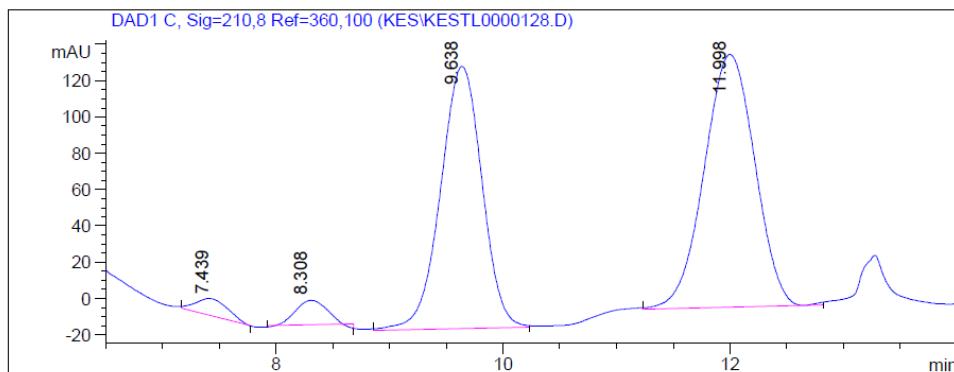
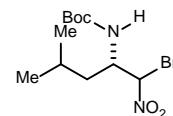
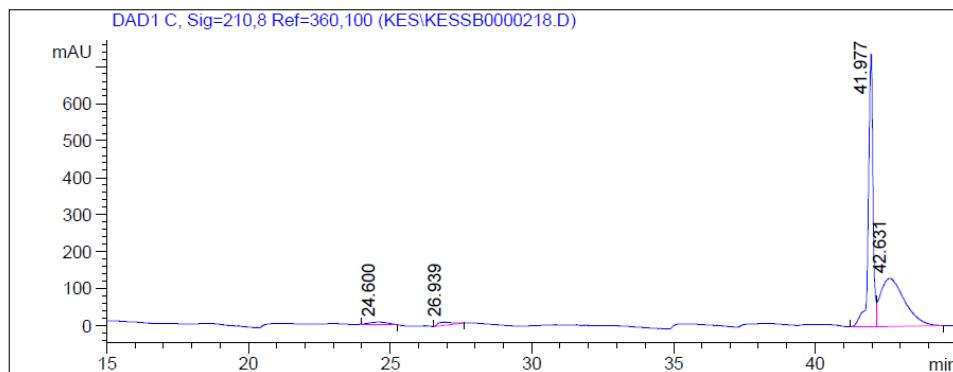
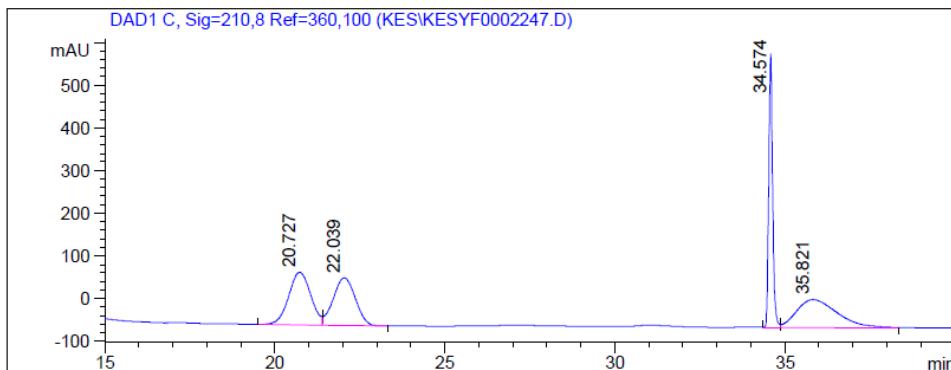
Figure 23. HPLC trace of *ent*-4f.

Figure 24. HPLC trace of *ent*-4g.¹

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

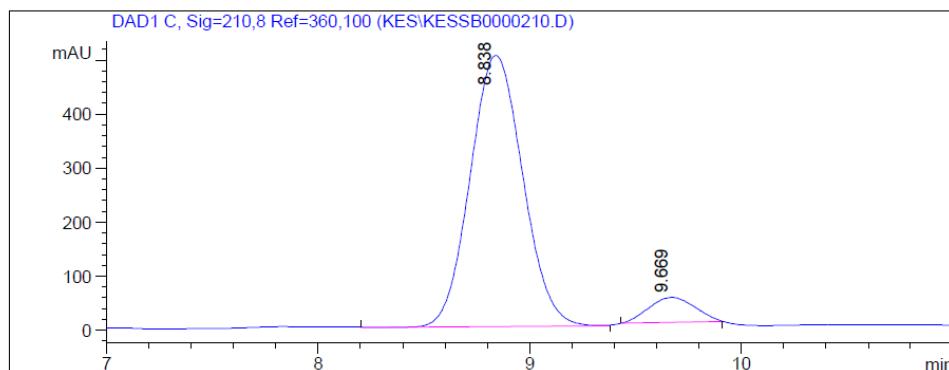
Peak #	RT [min]	Width [min]	Area	Area %
1	24.600	0.752	307.698	1.85
2	26.939	0.606	339.366	2.05
3	41.977	0.161	8267.955	49.82
4	42.631	0.881	7679.720	46.28



Signal 1: DAD1 C, Sig=210,8 Ref=360,100

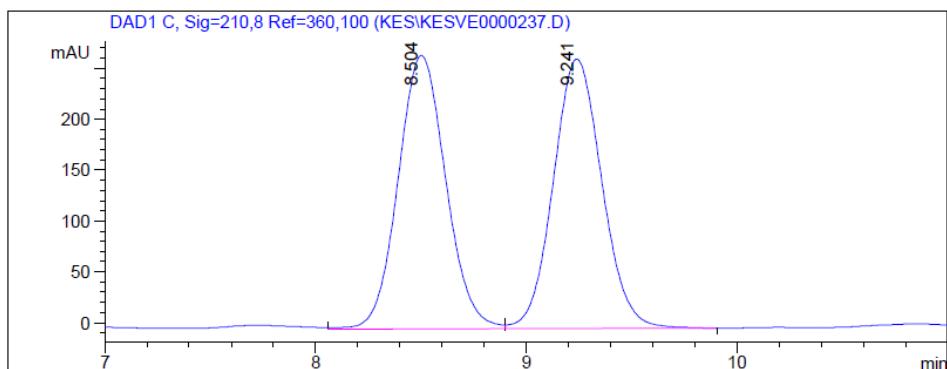
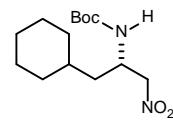
Peak #	RT [min]	Width [min]	Area	Area %
1	20.727	0.705	5527.214	26.05
2	22.039	0.708	5041.059	23.76
3	34.574	0.119	5125.187	24.15
4	35.821	1.204	5525.594	26.04

The variance in retention times is due to the very low polarity and slow flow rate of the mobile phase.

Figure 25. HPLC trace of *ent*-4h.

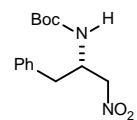
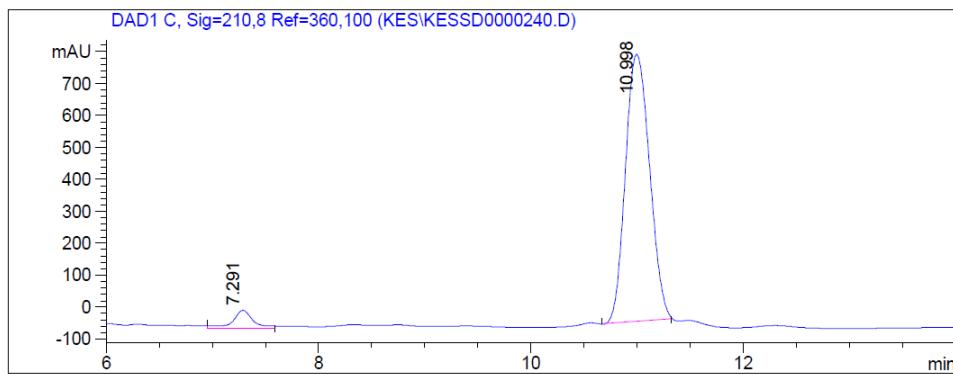
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	8.838	0.287	8664.856	92.54
2	9.669	0.252	698.467	7.46



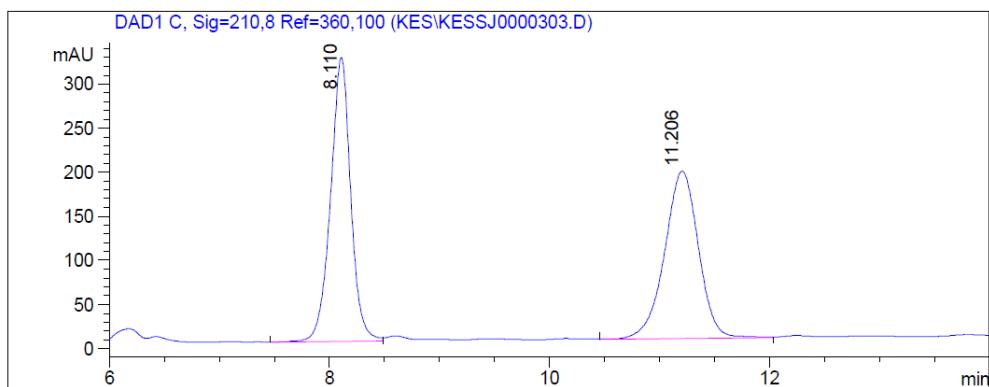
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	8.504	0.245	4223.312	49.88
2	9.241	0.251	4243.221	50.12

Figure 26. HPLC trace of *ent*-4i.¹

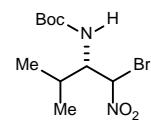
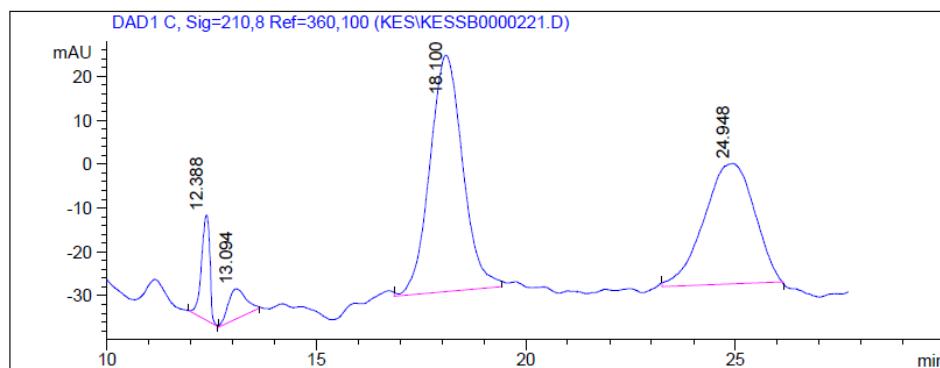
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	7.291	0.215	704.386	5.05
2	10.998	0.264	13245.113	94.95



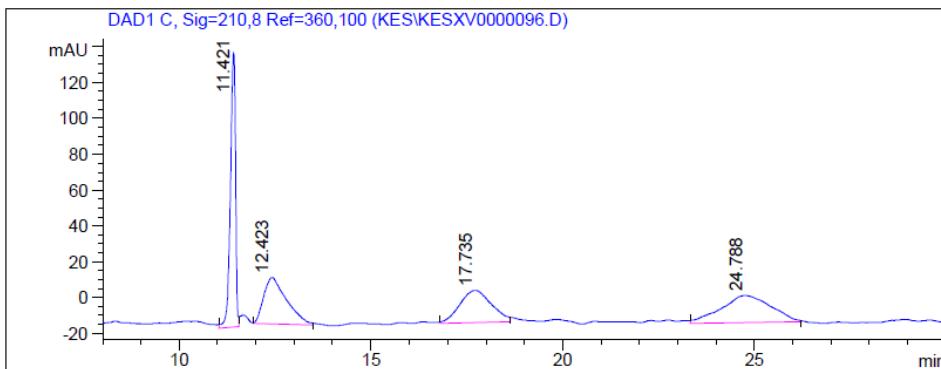
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	8.110	0.191	4114.355	50.24
2	11.206	0.328	4074.705	49.76

Figure 27. HPLC trace of *ent*-4j.

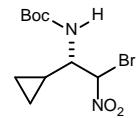
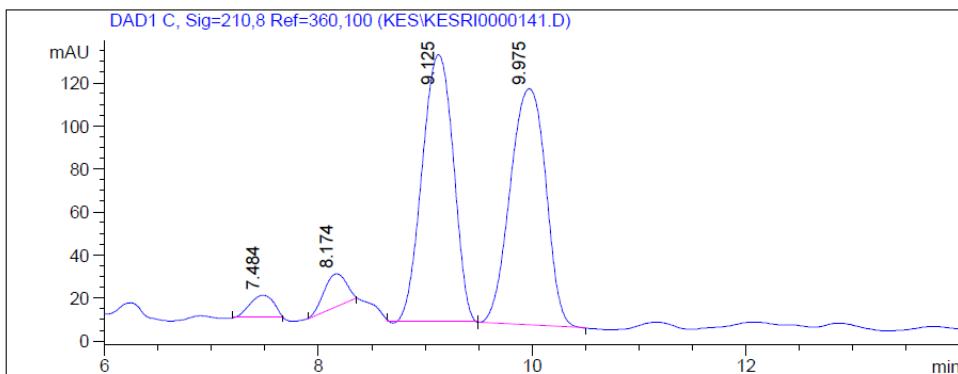
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	12.388	0.230	331.194	5.75
2	13.094	0.486	199.653	3.46
3	18.100	0.909	2936.744	50.95
4	24.948	1.395	2295.832	39.83



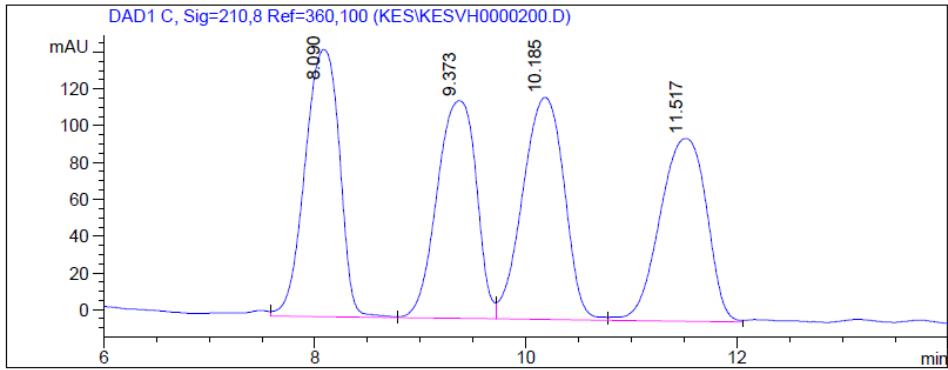
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	11.421	0.156	1431.929	29.05
2	12.423	0.693	1078.494	21.88
3	17.735	0.964	1040.948	21.12
4	24.788	1.510	1377.935	27.95

Figure 28. HPLC trace of *ent*-4k.¹

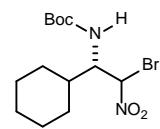
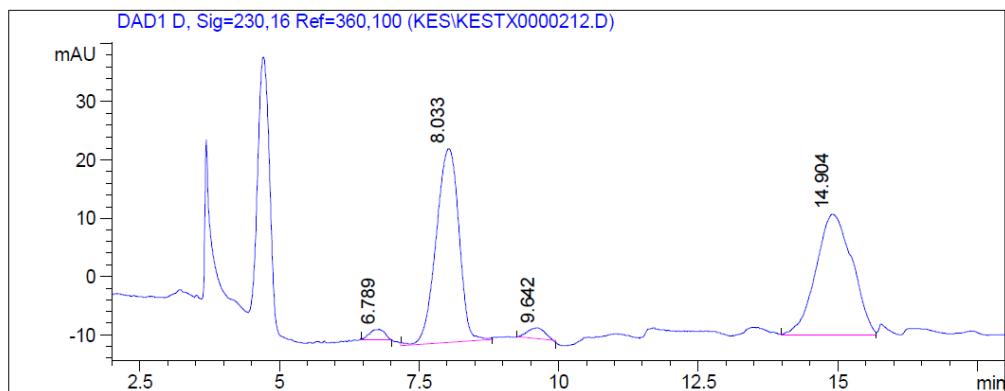
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
<hr/>				
1	7.484	0.259	160.949	2.96
2	8.174	0.242	222.676	4.09
3	9.125	0.339	2522.911	46.35
4	9.975	0.386	2536.927	46.61



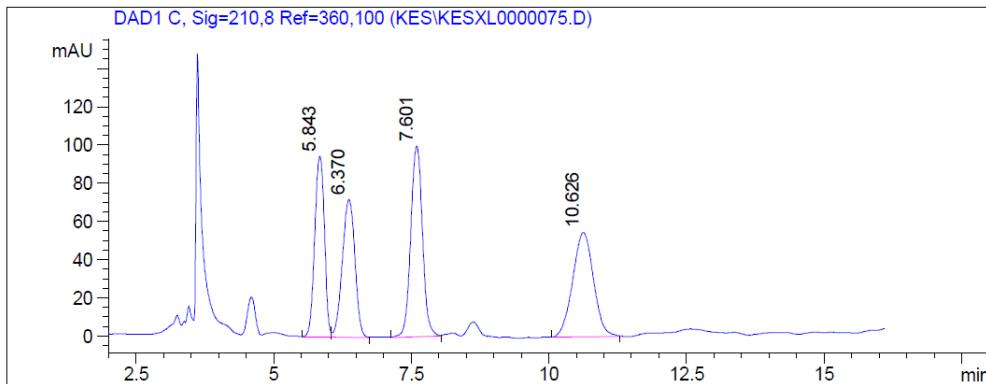
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
<hr/>				
1	8.090	0.370	3308.149	25.96
2	9.373	0.422	3063.356	24.04
3	10.185	0.444	3308.714	25.97
4	11.517	0.499	3060.615	24.02

Figure 29. HPLC trace of *ent*-4l.¹

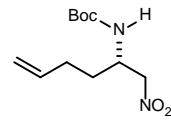
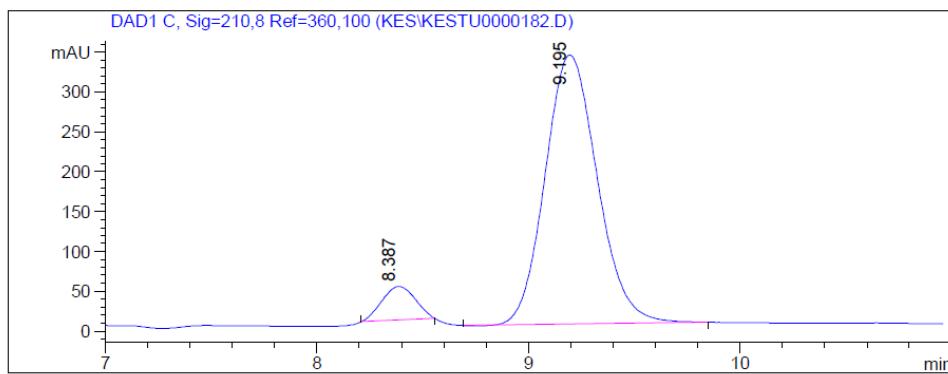
Signal 1: DAD1 D, Sig=230,16 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
<hr/>				
1	6.789	0.306	31.746	1.62
2	8.033	0.472	941.729	48.10
3	9.642	0.357	38.763	1.98
4	14.904	0.757	945.662	48.30
<hr/>				



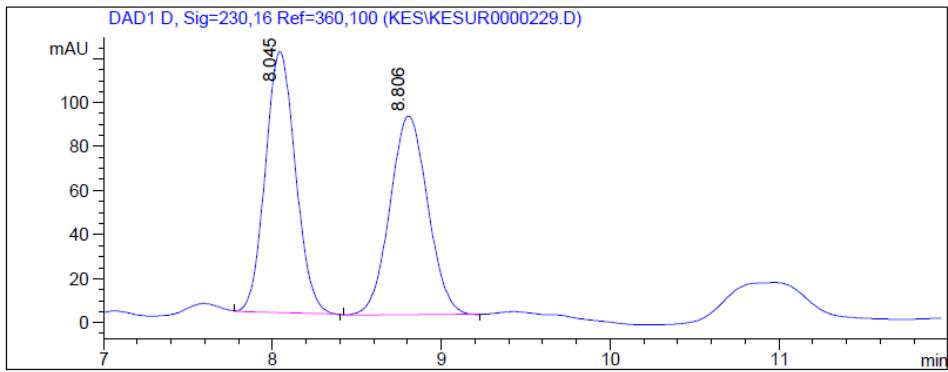
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
<hr/>				
1	5.843	0.205	1164.348	22.23
2	6.370	0.266	1151.221	21.98
3	7.601	0.247	1483.777	28.33
4	10.626	0.438	1437.213	27.45
<hr/>				

Figure 30. HPLC trace of *ent*-4m.

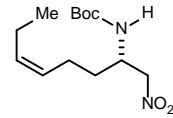
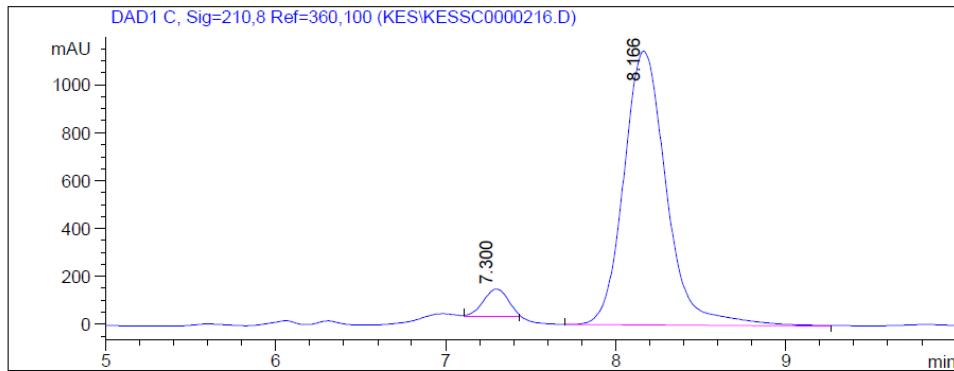
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	8.387	0.184	462.373	7.39
2	9.195	0.286	5793.555	92.61



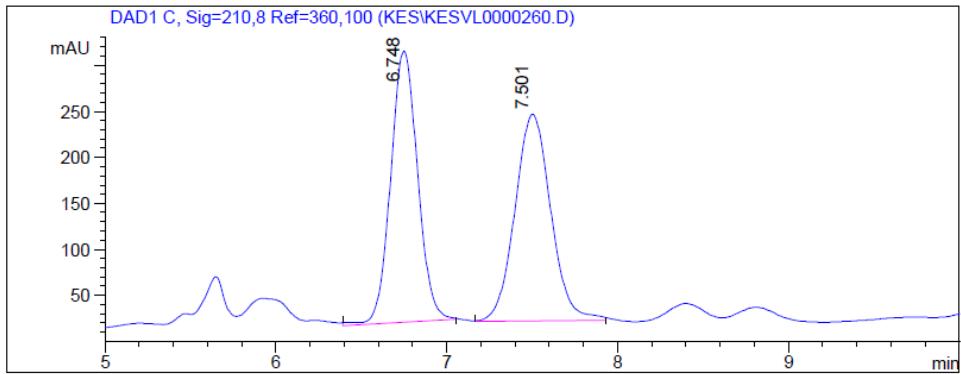
Signal 1: DAD1 D, Sig=230,16 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	8.045	0.207	1473.206	51.15
2	8.806	0.260	1406.843	48.85

Figure 31. HPLC trace of *ent*-4n.

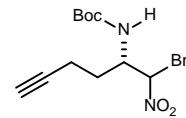
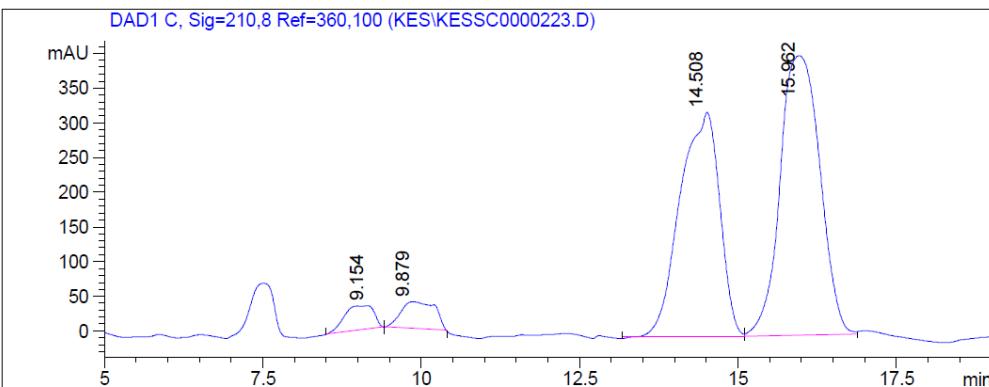
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	7.300	0.166	1140.891	5.41
2	8.166	0.290	19953.918	94.59



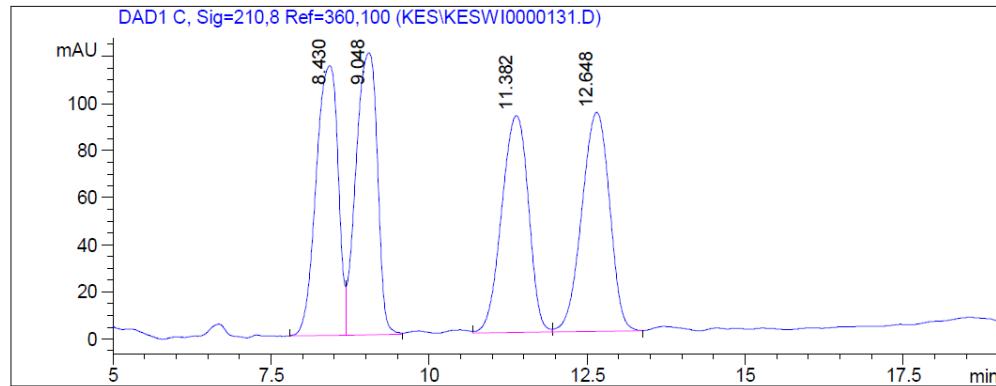
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	6.748	0.183	3230.231	49.58
2	7.501	0.243	3284.427	50.42

Figure 32. HPLC trace of *ent*-4o.¹

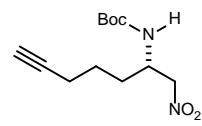
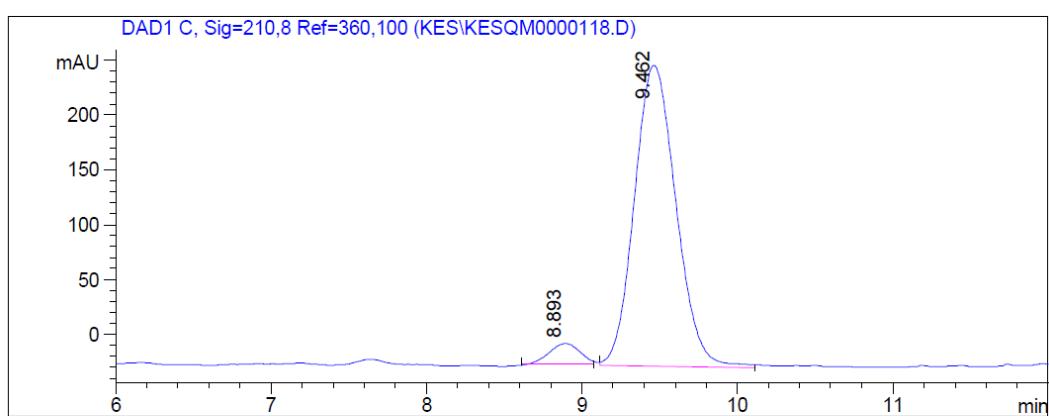
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	9.154	0.559	1109.961	3.25
2	9.879	0.629	1446.043	4.23
3	14.508	0.721	13954.747	40.85
4	15.962	0.730	17649.492	51.67



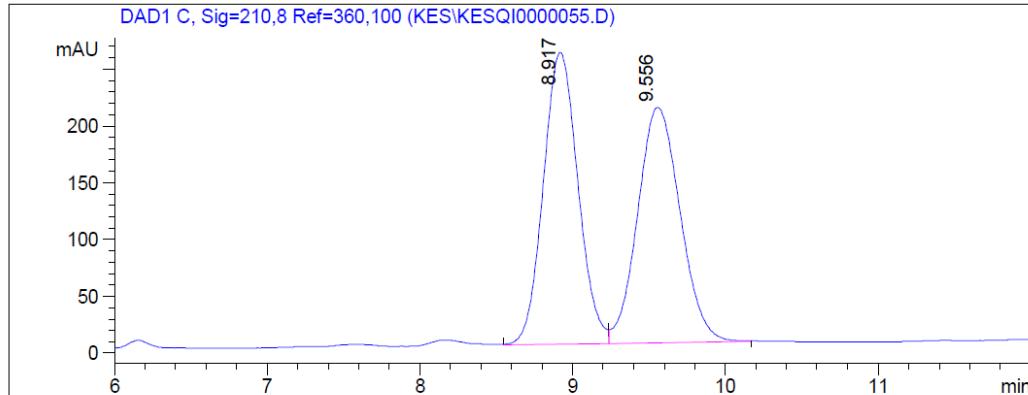
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	8.430	0.390	2768.777	24.82
2	9.048	0.385	2826.707	25.34
3	11.382	0.472	2715.929	24.35
4	12.648	0.489	2841.800	25.48

Figure 33. HPLC trace of *ent*-4p.

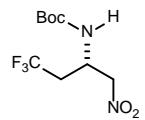
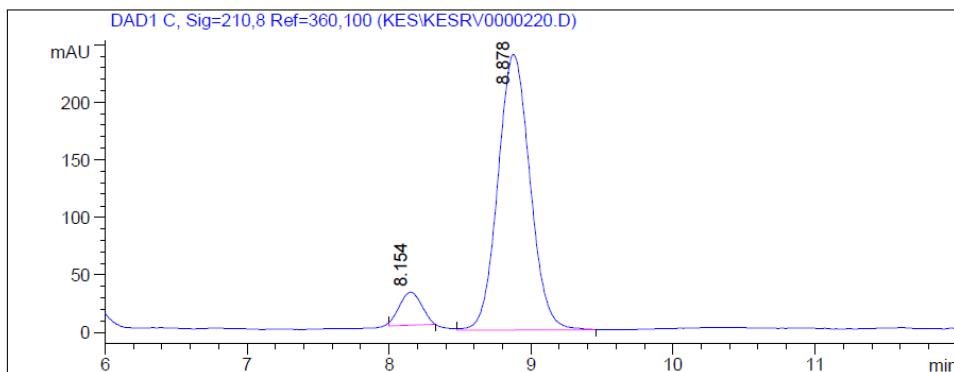
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	8.893	0.220	241.381	4.51
2	9.462	0.310	5107.460	95.49



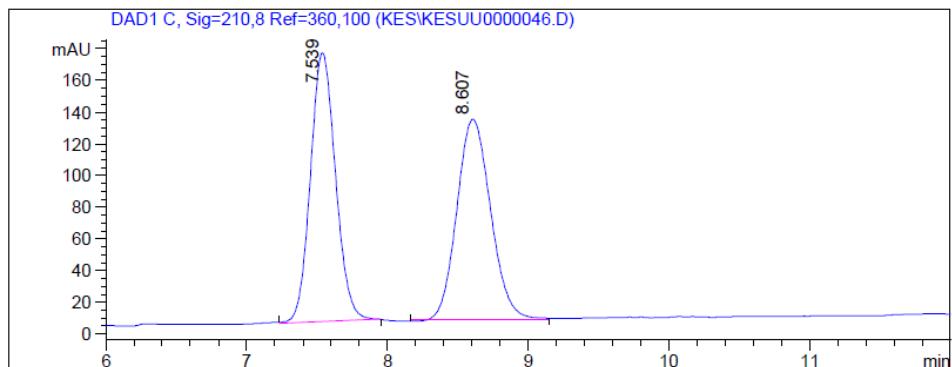
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	8.917	0.246	4057.678	50.24
2	9.556	0.302	4019.170	49.76

Figure 34. HPLC trace of *ent*-4q.

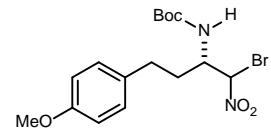
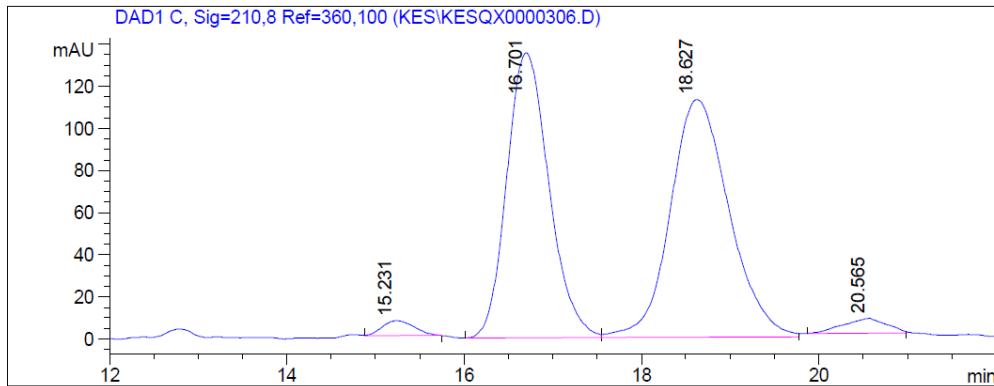
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	8.154	0.180	310.004	7.61
2	8.878	0.245	3762.993	92.39



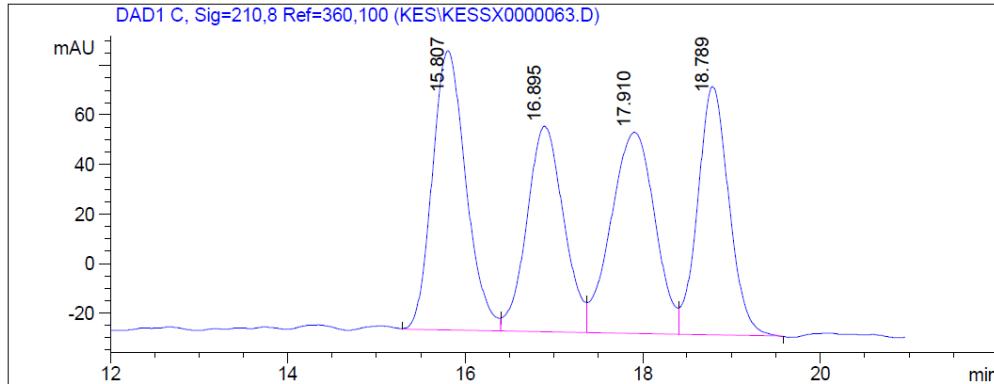
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	7.539	0.207	2098.937	50.08
2	8.607	0.277	2092.085	49.92

Figure 35. HPLC trace of *ent*-4r.¹

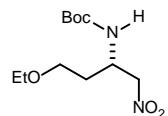
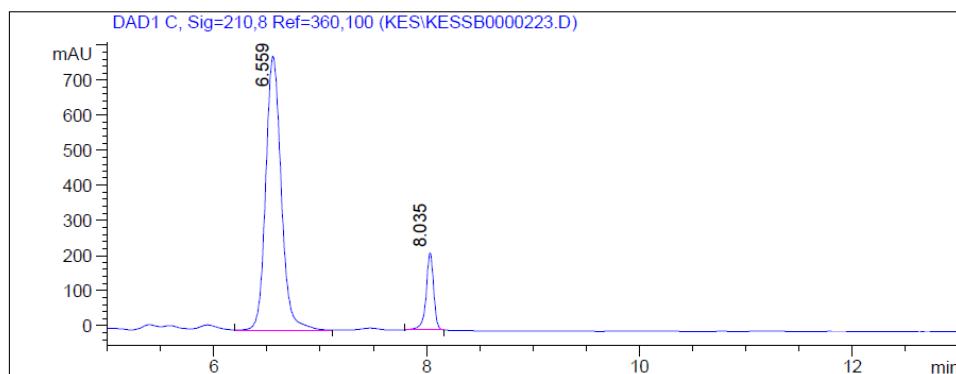
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	15.231	0.408	175.302	1.74
2	16.701	0.510	4479.730	44.36
3	18.627	0.693	5206.663	51.56
4	20.565	0.562	236.617	2.34



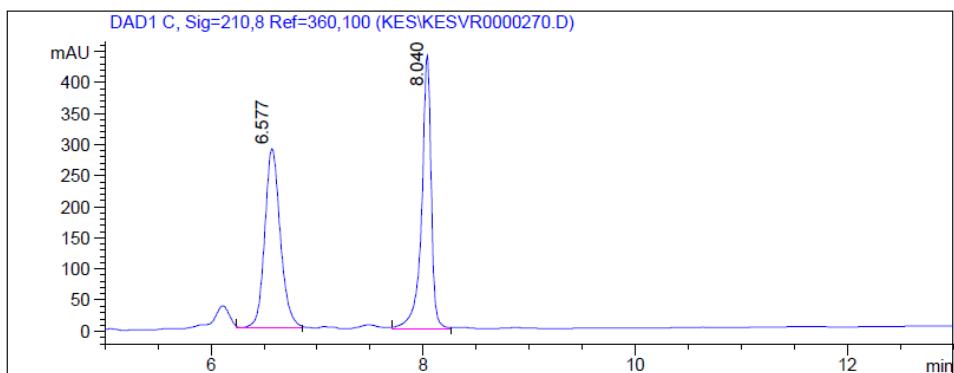
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	15.807	0.438	2964.389	27.96
2	16.895	0.481	2395.919	22.60
3	17.910	0.572	2789.024	26.31
4	18.789	0.408	2452.660	23.13

Figure 36. HPLC trace of *ent*-4s.

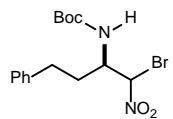
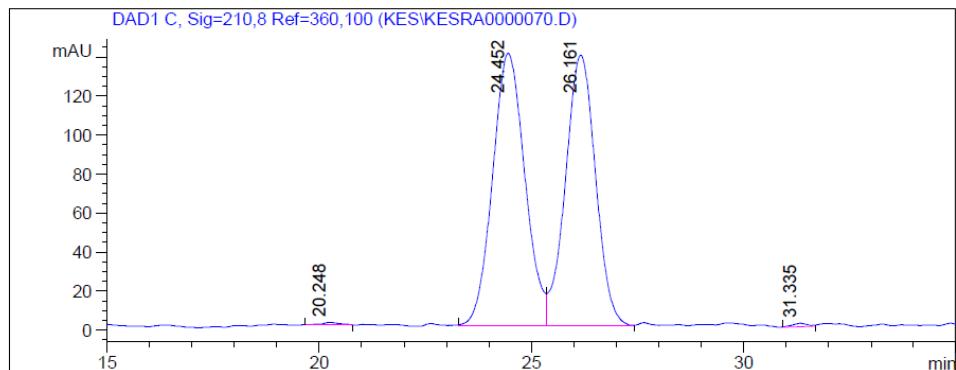
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	6.559	0.168	7877.934	88.09
2	8.035	0.081	1064.871	11.91



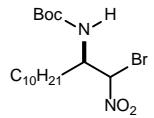
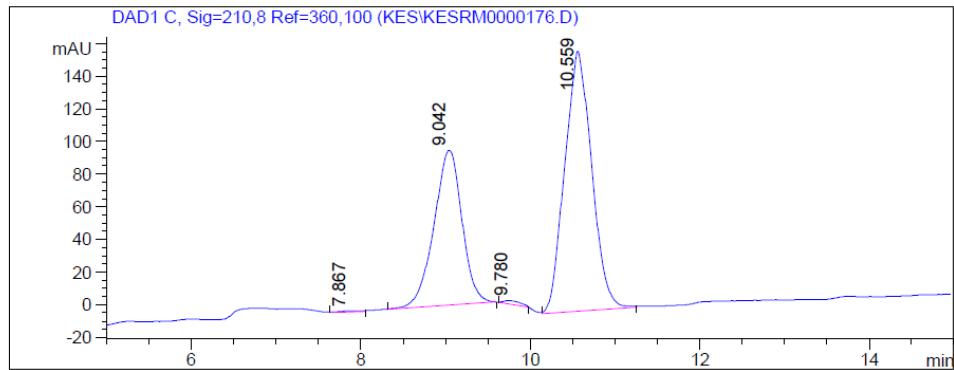
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	6.577	0.170	2928.512	51.42
2	8.040	0.105	2766.864	48.58

Figure 37. HPLC trace of recrystallized **4a**.

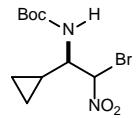
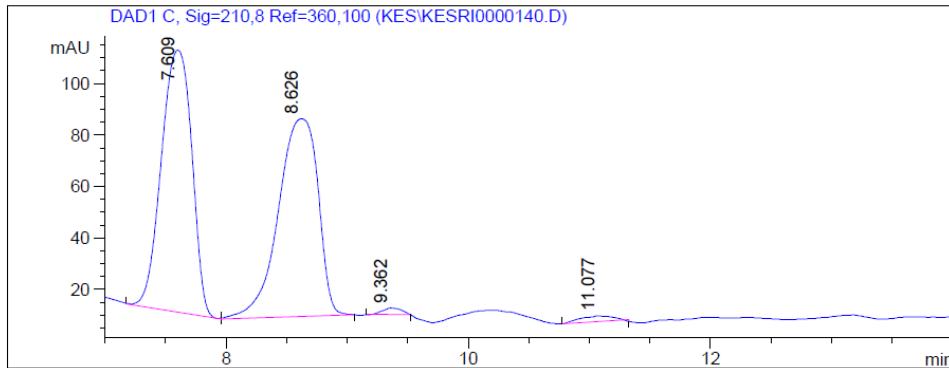
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	20.248	0.403	30.912	0.22
2	24.452	0.794	7368.515	51.65
3	26.161	0.751	6822.053	47.82
4	31.335	0.416	45.350	0.32

Figure 38. HPLC trace of recrystallized **4e**.

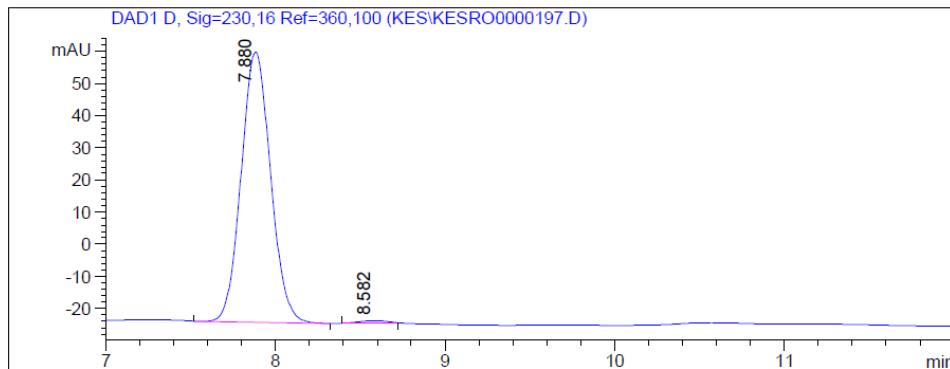
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	7.867	0.222	11.722	0.20
2	9.042	0.382	2168.692	37.85
3	9.780	0.238	30.617	0.53
4	10.559	0.368	3518.577	61.41

Figure 39. HPLC trace of recrystallized **4k**.

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	7.609	0.293	1793.364	49.48
2	8.626	0.381	1758.631	48.52
3	9.362	0.183	28.413	0.78
4	11.077	0.316	43.831	1.21

Figure 40. HPLC trace of recrystallized **4m**.

Signal 1: DAD1 D, Sig=230,16 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
<hr/>				
1	7.880	0.201	1016.557	99.30
2	8.582	0.167	7.181	0.70

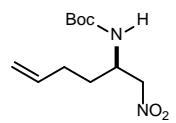
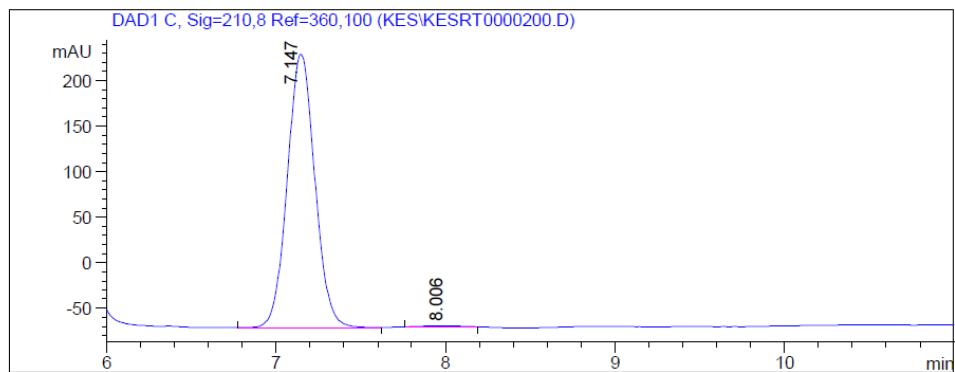


Figure 41. HPLC trace of recrystallized **4n**.

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	7.147	0.189	3420.135	99.47
2	8.006	0.240	18.322	0.53

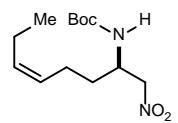
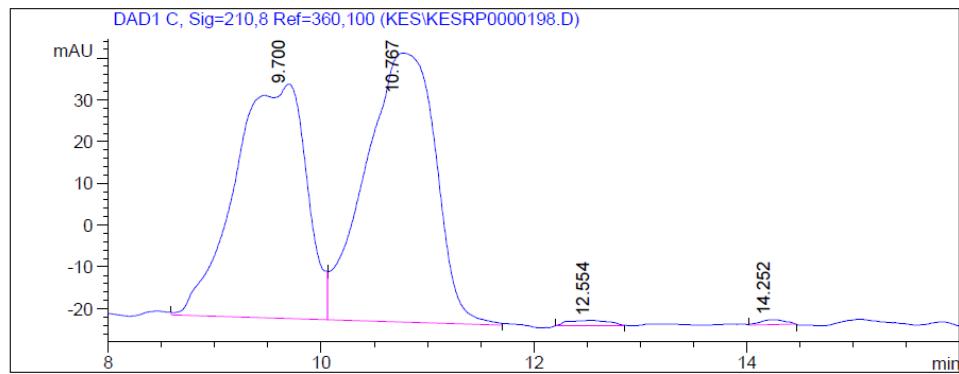


Figure 42. HPLC trace of recrystallized **4o**.

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	9.700	0.779	2627.294	46.70
2	10.767	0.762	2944.007	52.33
3	12.554	0.448	36.075	0.64
4	14.252	0.257	18.020	0.32

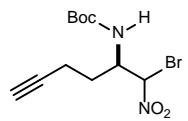
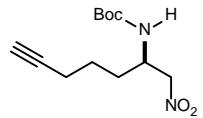
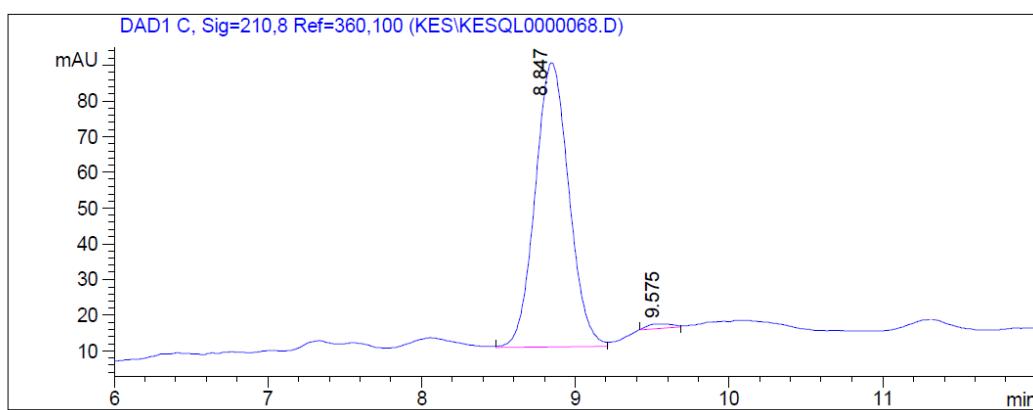


Figure 43. HPLC trace of recrystallized **4p**.

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Width [min]	Area	Area %
1	8.847	0.254	1213.172	98.89
2	9.575	0.194	13.588	1.11

References:

¹ Assays for racemic and enantioenriched samples were often separated by months or years. Relative retention times, however, are highly consistent. Changes in absolute retention times can be caused by 1) extensive column use, 2) column replacement, or 3) differences in ambient temperature. In some cases, low flow rates and low polarity eluent use lead to more variable absolute retention times. In all cases, the measured er's translate directly to measured dr for the UmAS product, further corroborating the measurements.

² Palomo, C.; Oiarbide, M.; Laso, A.; López, R. *J. Am. Chem. Soc.* **2005**, 127, 17622