

## Supporting Information

### CATALYTIC ENANTIOSELECTIVE DESYMMETRIZATION OF *meso*-AZIRIDINES WITH FLUOROMALONATES

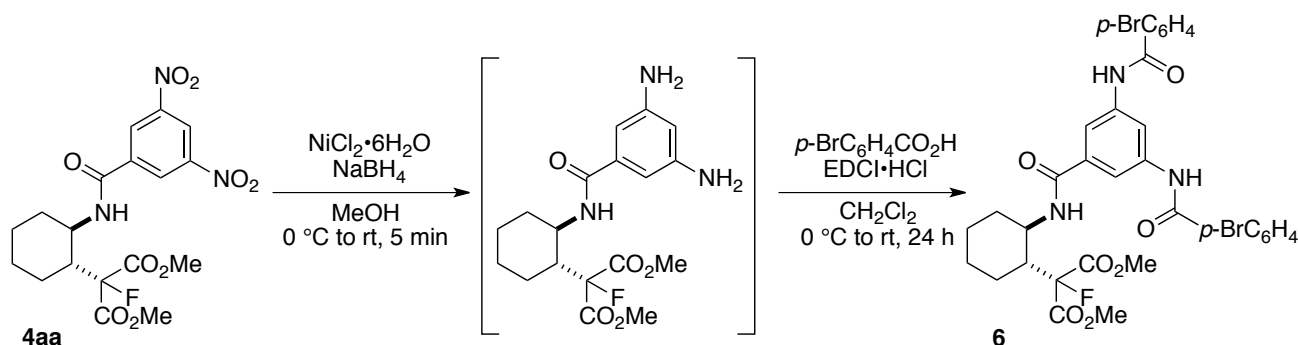
Seiya Fukagawa,<sup>a</sup> Yingjie Xu,<sup>b</sup> Masahiro Anada,<sup>a</sup> Tatsuhiko Yoshino,<sup>a,\*</sup> and Shigeki Matsunaga<sup>a,\*</sup>

<sup>a</sup> Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo 060-0812, Japan.

E-mail: smatsuna@pharm.hokudai.ac.jp

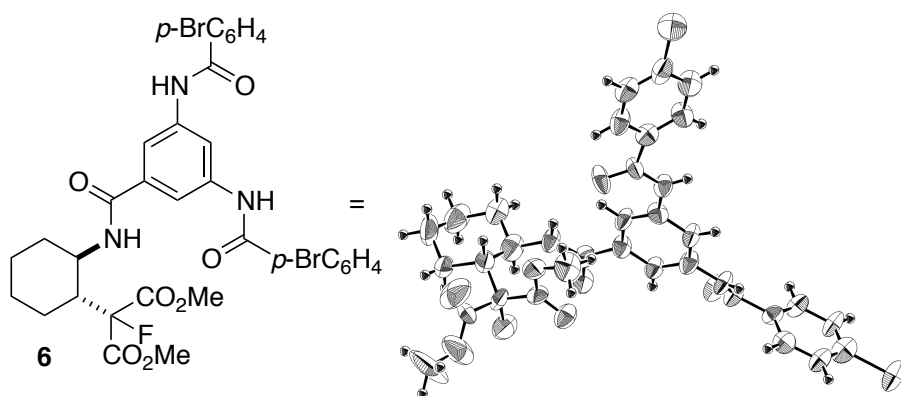
<sup>b</sup> Graduate School of Pharmaceutical Sciences, the University of Tokyo, Hongo, Tokyo, Japan.

#### [Synthesis of compound 6 for X-ray Analysis]



**Dimethyl 2-((1*R*,2*R*)-2-(3,5-bis(4-bromobenzamido)benzamido)cyclohexyl)-2-fluoromalonate (6):** To a stirred suspension of **4aa** (37.1 mg, 0.084 mmol) in MeOH (1.5 ml) was added NiCl<sub>2</sub>·6H<sub>2</sub>O (40 mg, 0.17 mmol) at 0 °C. Then, the mixture was added NaBH<sub>4</sub> (64 mg, 1.7 mmol) in several portions and stirred for 5 min at 0 °C. The reaction mixture was quenched by NH<sub>4</sub>Cl and diluted with CH<sub>2</sub>Cl<sub>2</sub>. The organic layer was separated, and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> and AcOEt. Combined organic phases were dried over Na<sub>2</sub>SO<sub>4</sub>, filtration and evaporation. The obtained crude mixture dissolved in CH<sub>2</sub>Cl<sub>2</sub>, and the mixture was added *p*-bromobenzoic acid (38 mg, 0.19 mmol) and EDCI·HCl (48 mg, 0.25 mmol) at 0 °C. Then, the mixture was allowed to warm to room temperature and stirred for 24 h. The reaction mixture was diluted with AcOEt and H<sub>2</sub>O, and the organic layer was separated. The aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> and AcOEt, and combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>. After filtration and evaporation, the obtained crude mixture was purified by silica gel column chromatography (AcOEt/hexane = 1:1) to afford **6** (37.5 mg, 60% yield in 2 steps); colorless solid, <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 1.05-1.44 (m, 4H), 1.44-1.83 (m, 4H), 2.50-2.71 (m, 1H), 3.43 (s, 3H), 3.76 (s, 3H), 3.87-4.00 (m, 1H), 6.77 (d, *J* = 9.5

Hz, 1H), 7.49 (d,  $J = 8.2$  Hz, 4H), 7.70 (d,  $J = 8.2$  Hz, 4H), 8.02 (d,  $J = 1.2$ , 2H), 8.38 (brs, 1H), 9.35 (brs, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  24.7, 25.0, 26.4, 33.9, 46.6 (d,  $J_{\text{C-F}} = 21.0$  Hz), 48.2, 53.5, 96.0 (d,  $J_{\text{C-F}} = 209$  Hz), 115.0, 115.5, 126.7, 129.0, 131.7, 133.2, 135.2, 139.2, 165.7, 166.0, 166.2 (d,  $J_{\text{C-F}} = 25.7$  Hz), 167.4 (d,  $J_{\text{C-F}} = 24.8$  Hz); HRMS (ESI):  $m/z$  calculated for  $\text{C}_{32}\text{H}_{30}\text{O}_7\text{N}_3\text{Br}_2\text{FNa}^+$   $[\text{M}+\text{Na}]^+$ : 768.0327, found: 768.0331

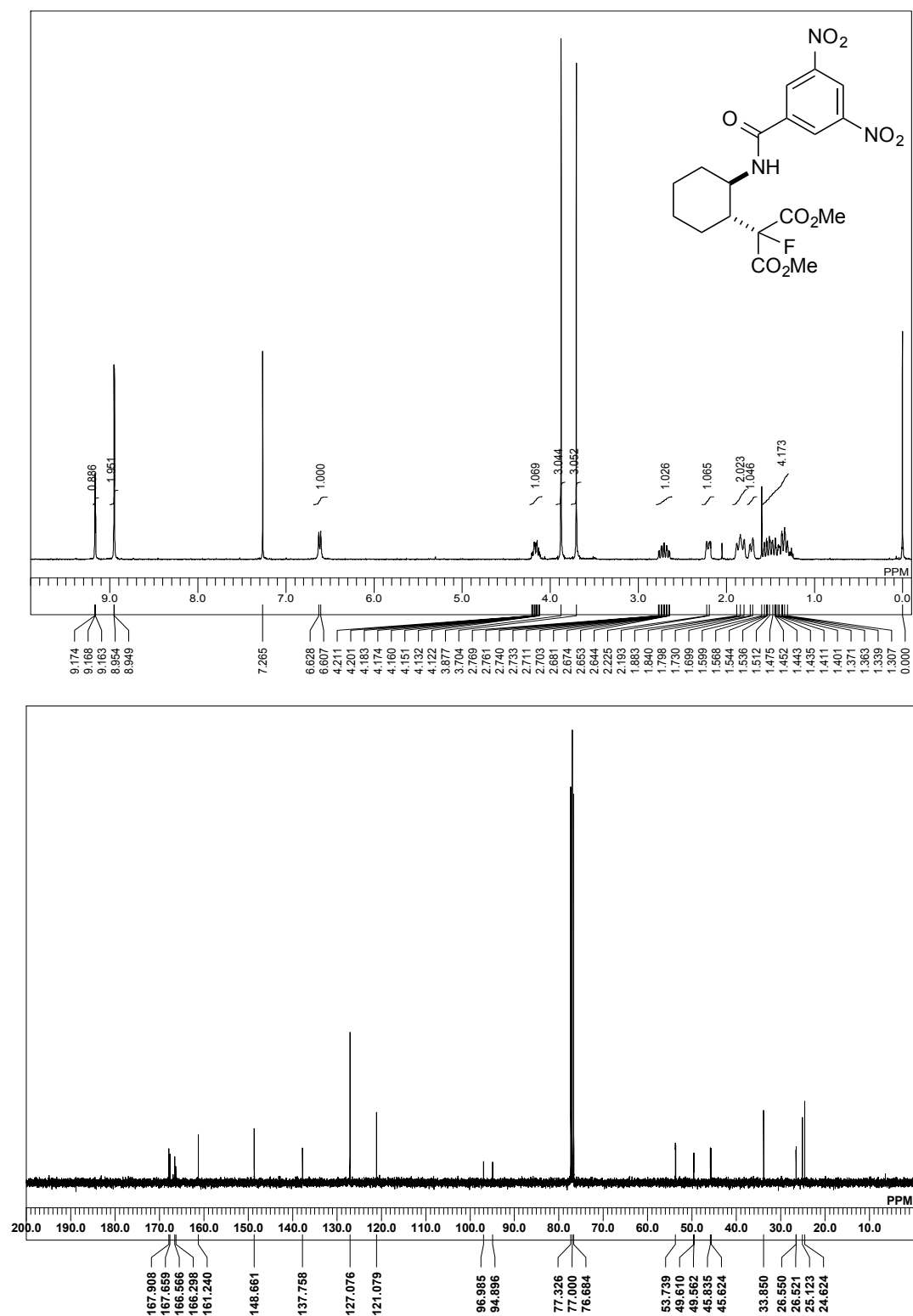


**Table. Crystal data and structure refinement for compound 6.**

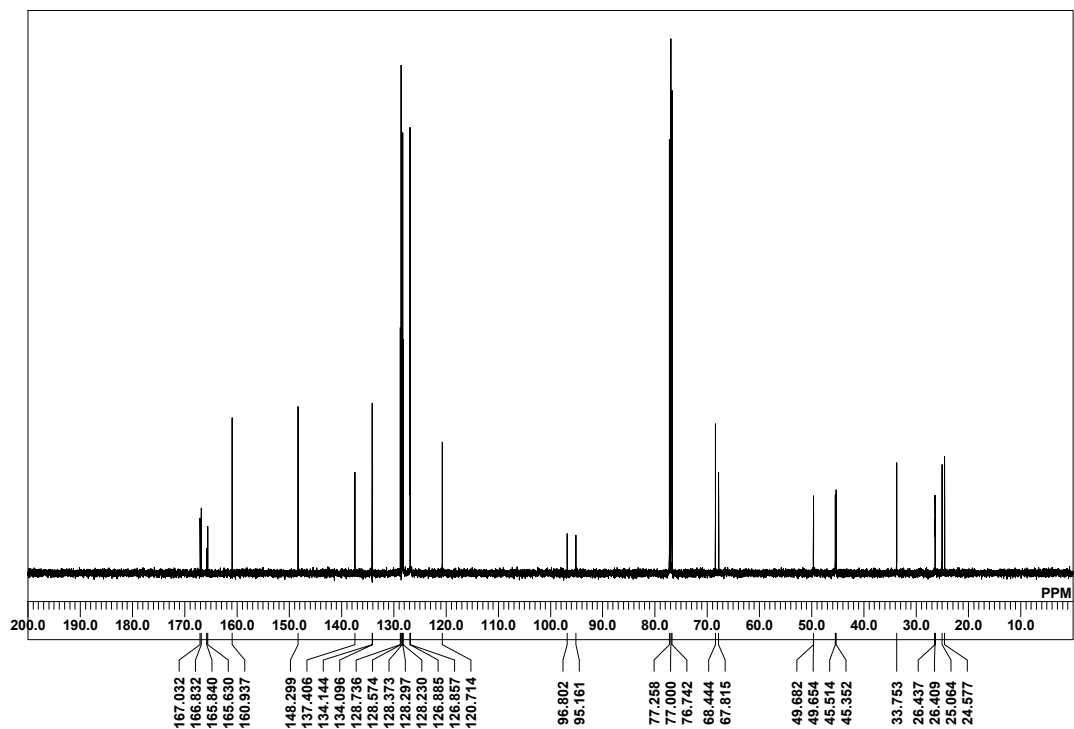
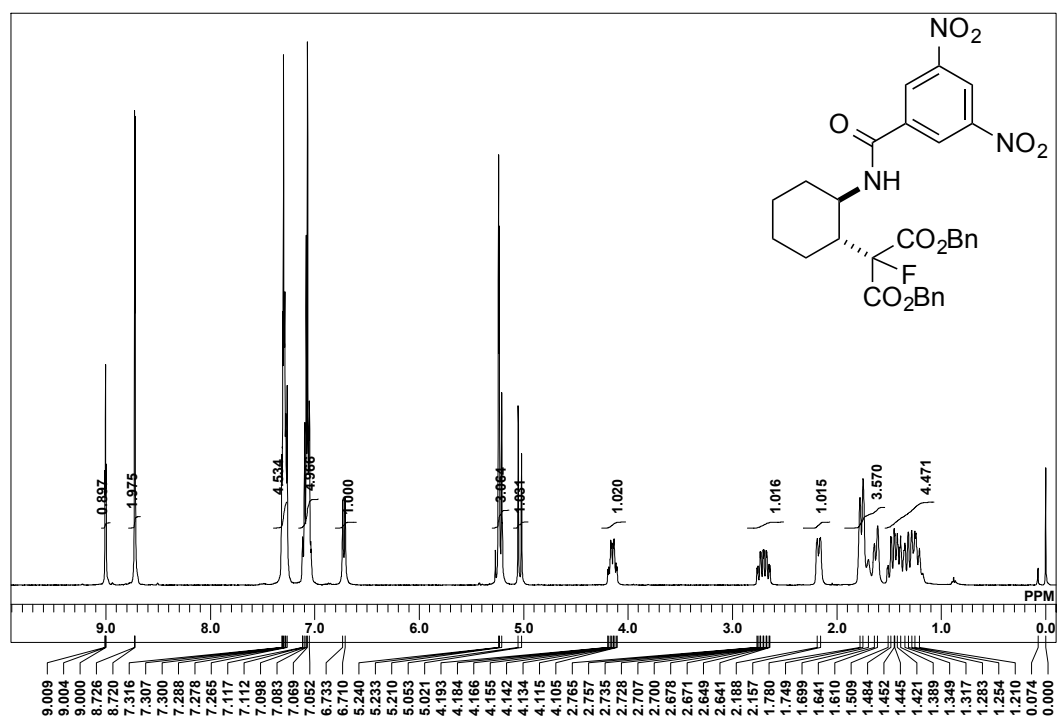
Identification code	ty01	
Empirical formula	$\text{C}_{34}\text{H}_{40}\text{Br}_2\text{F}\text{N}_3\text{O}_{10}$	
Formula weight	829.51	
Temperature	133(2) K	
Wavelength	1.54187 Å	
Crystal system	Trigonal	
Space group	P 31	
Unit cell dimensions	$a = 17.5493(13)$ Å	$a = 90^\circ$ .
	$b = 17.5493(13)$ Å	$b = 90^\circ$ .
	$c = 10.6154(4)$ Å	$g = 120^\circ$ .
Volume	$2831.3(3)$ Å <sup>3</sup>	
Z	3	
Density (calculated)	1.460 Mg/m <sup>3</sup>	
Absorption coefficient	$3.257\text{ mm}^{-1}$	
F(000)	1272	
Crystal size	0.20 x 0.12 x 0.08 mm <sup>3</sup>	
Theta range for data collection	5.04 to 68.07°.	
Index ranges	$-21 \leq h \leq 20$ , $-21 \leq k \leq 21$ , $-12 \leq l \leq 12$	
Reflections collected	37327	

Independent reflections	6478 [R(int) = 0.1072]
Completeness to theta = 68.07°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.0000 and 0.5784
Refinement method	Full-matrix least-squares on F <sup>2</sup>
Data / restraints / parameters	6478 / 2 / 478
Goodness-of-fit on F <sup>2</sup>	1.037
Final R indices [I>2sigma(I)]	R1 = 0.0817, wR2 = 0.1605
R indices (all data)	R1 = 0.1486, wR2 = 0.1875
Absolute structure parameter	0.07(3)
Largest diff. peak and hole	0.678 and -0.300 e.Å <sup>-3</sup>

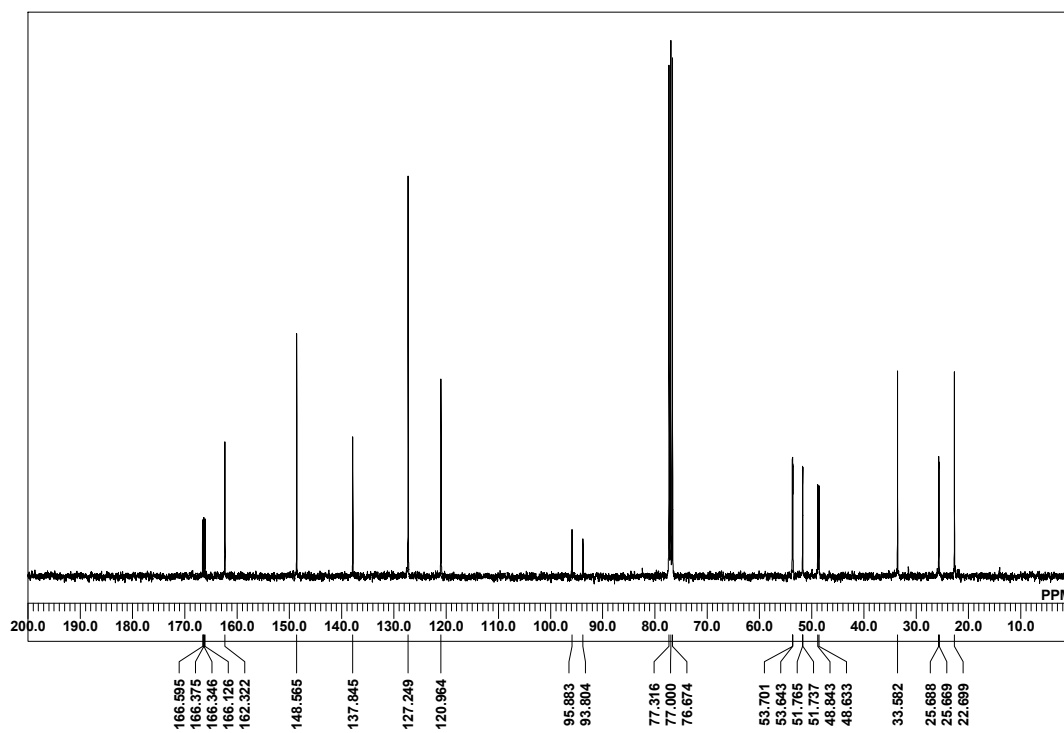
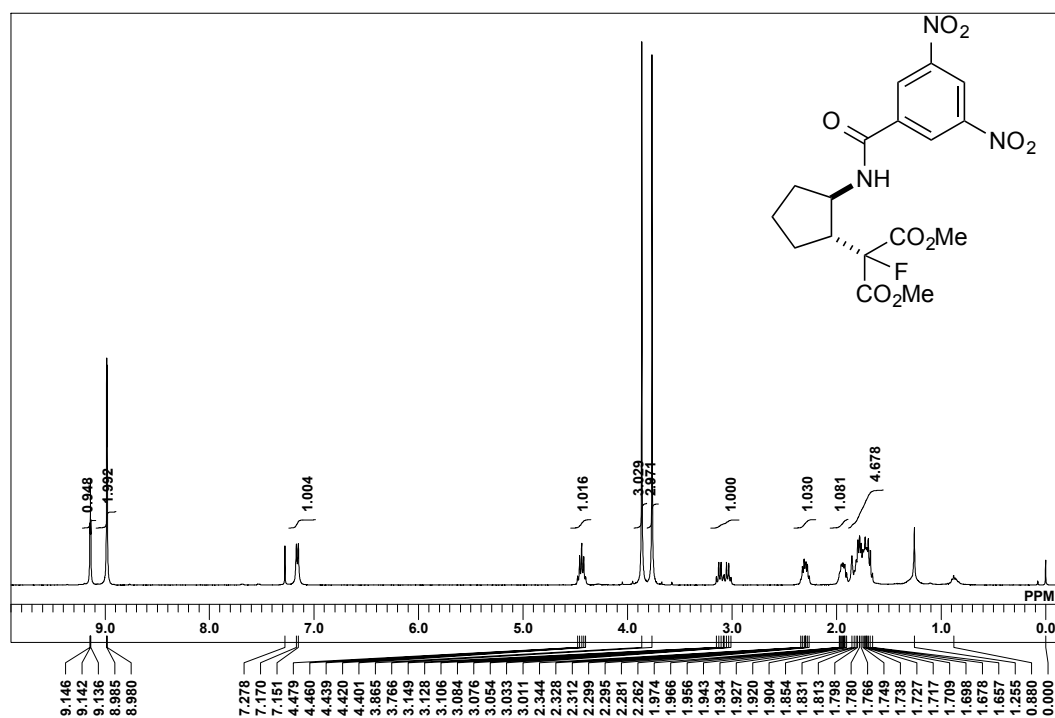
Dimethyl 2-((1*R*,2*R*)-2-(3,5-dinitrobenzamido)cyclohexyl)-2-fluoromalonate (4aa)



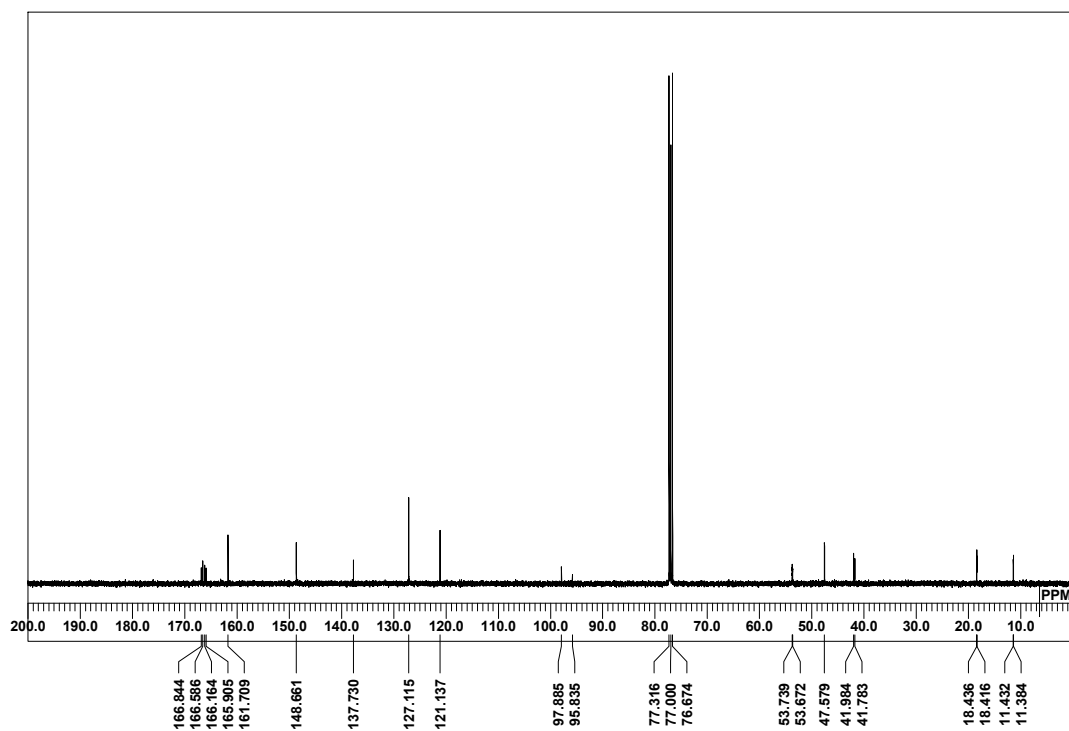
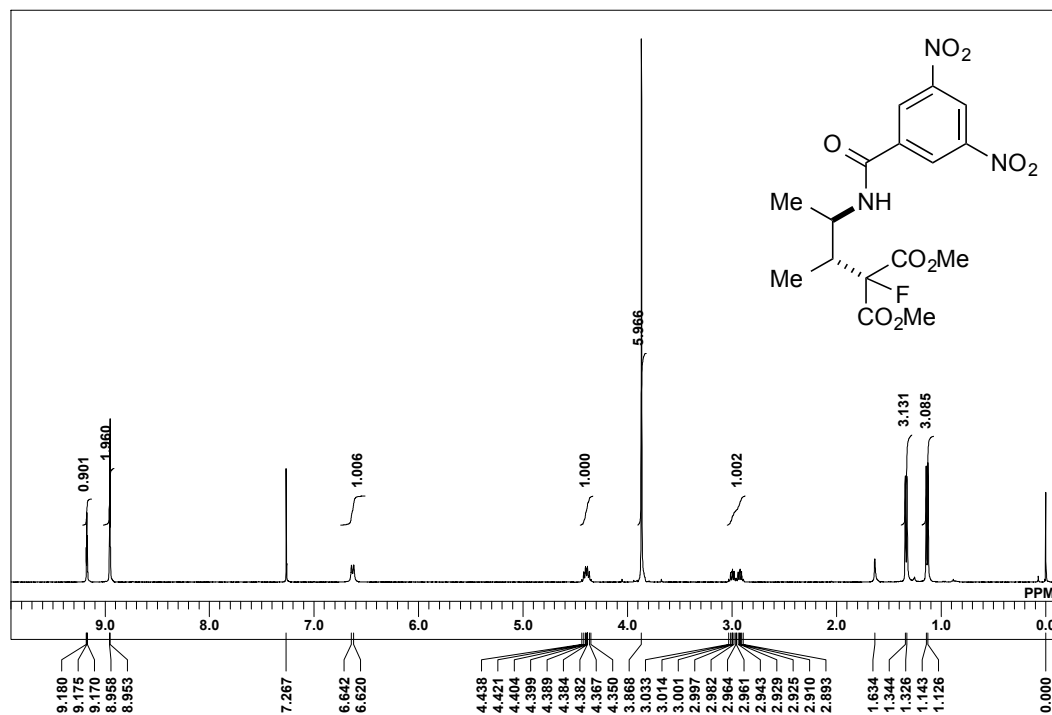
Dibenzyl 2-((1*R*,2*R*)-2-(3,5-dinitrobenzamido)cyclohexyl)-2-fluoromalonate (4b)



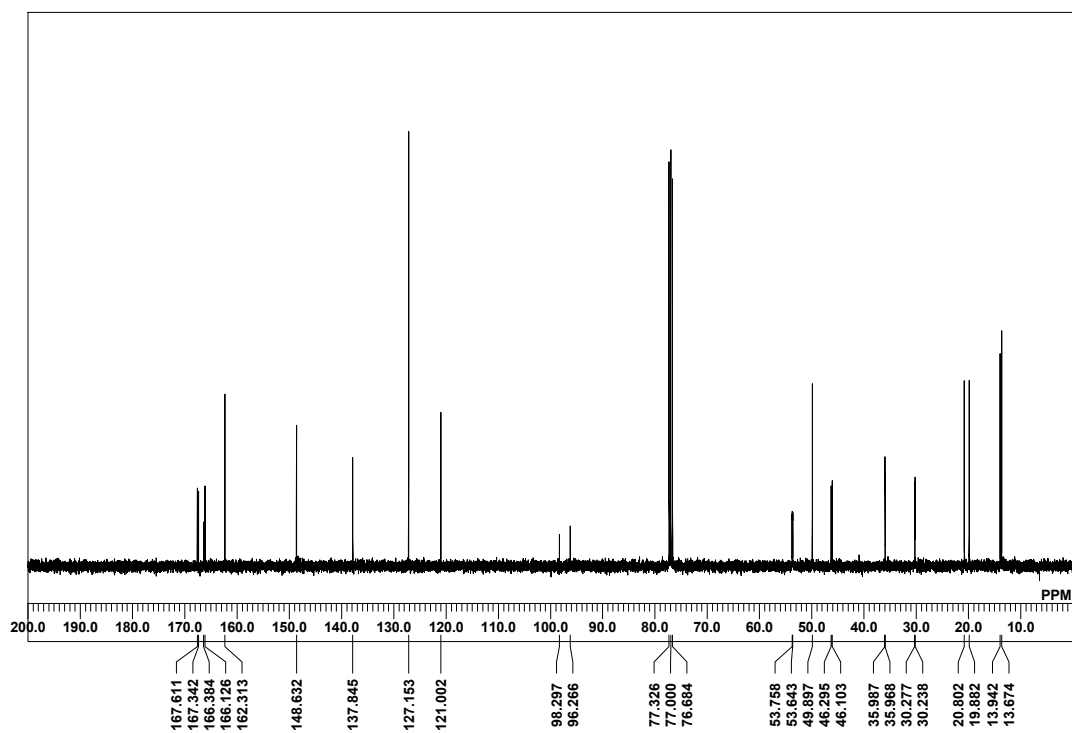
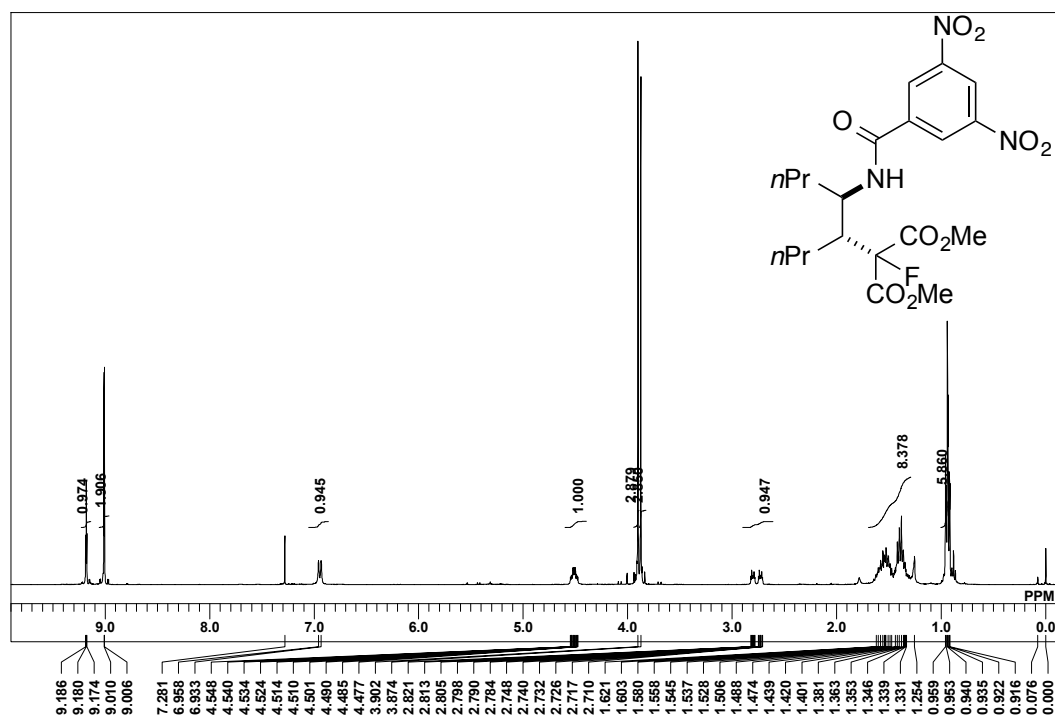
Dimethyl 2-((1*R*,2*R*)-2-(3,5-dinitrobenzamido)cyclopentyl)-2-fluoromalonate (4ba)



Dimethyl 2-((1*R*,2*R*)-3-(3,5-dinitrobenzamido)butan-4-yl)-2-fluoromalonate(4ca)



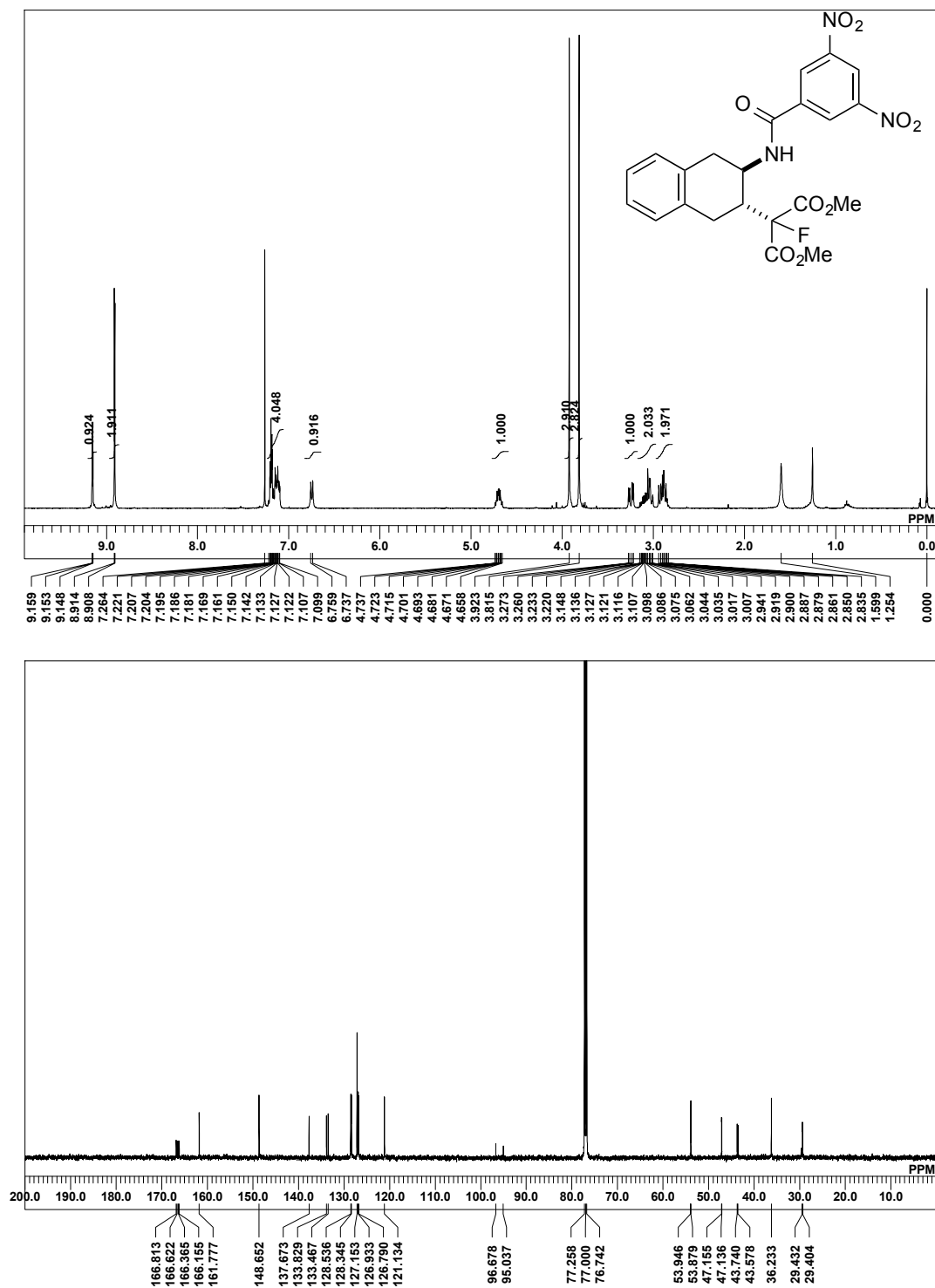
Dimethyl 2-((4*R*,5*R*)-5-(3,5-dinitrobenzamido)octane-4-yl)-2-fluoromalonate (4da)





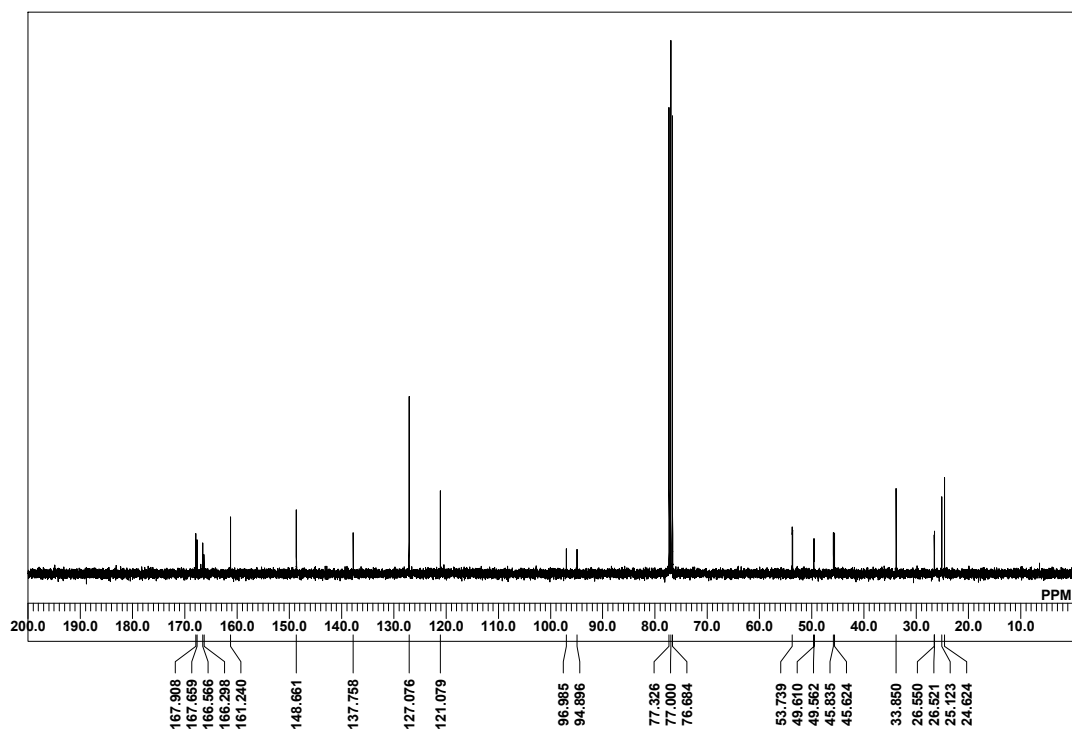
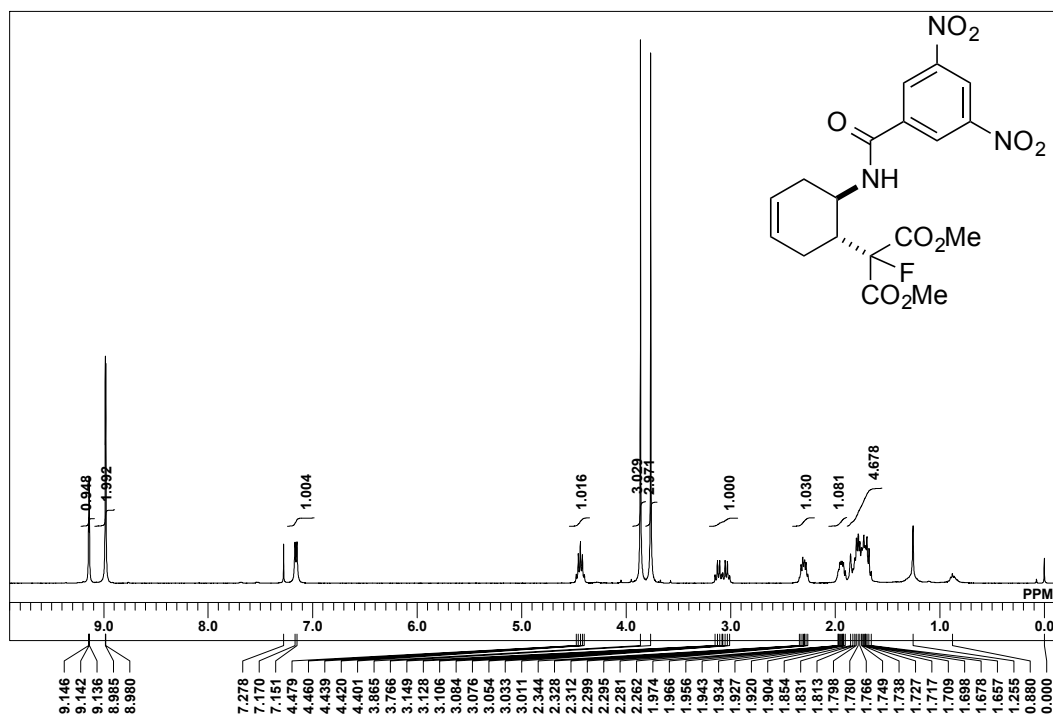
Dimethyl

2-((2*R*,3*R*)-3-(3,5-dinitrobenzamido)1,2,3,4-tetrahydronaphthalen-2-yl)-2-fluoroma  
lonate (4ea)

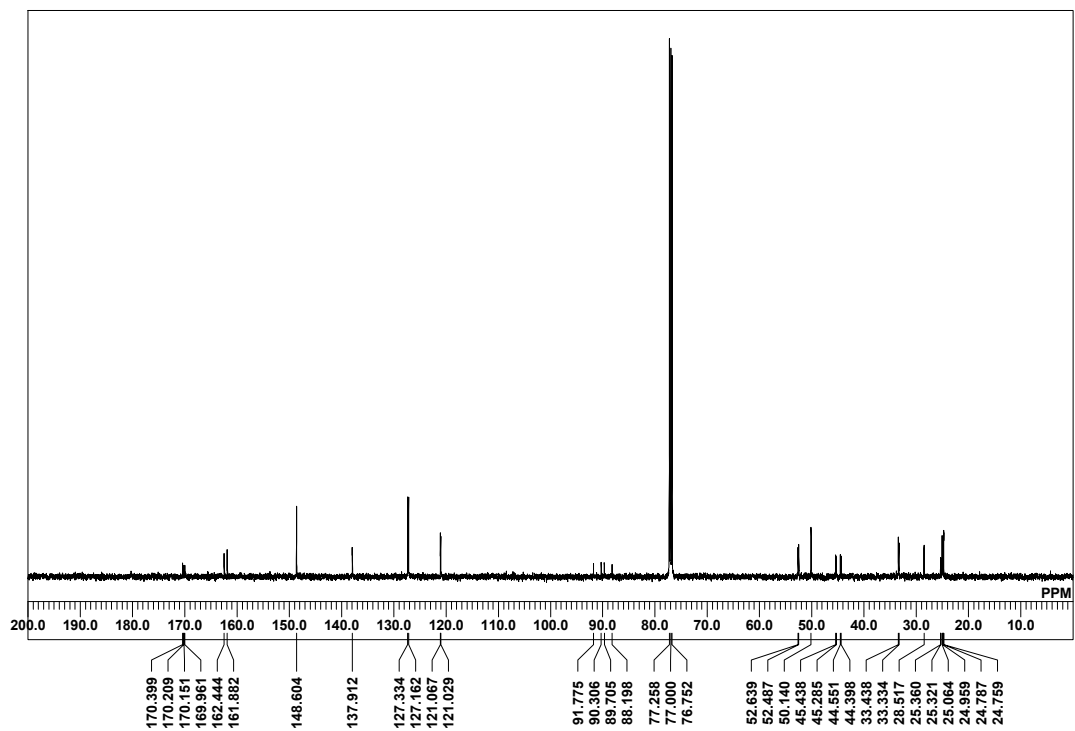
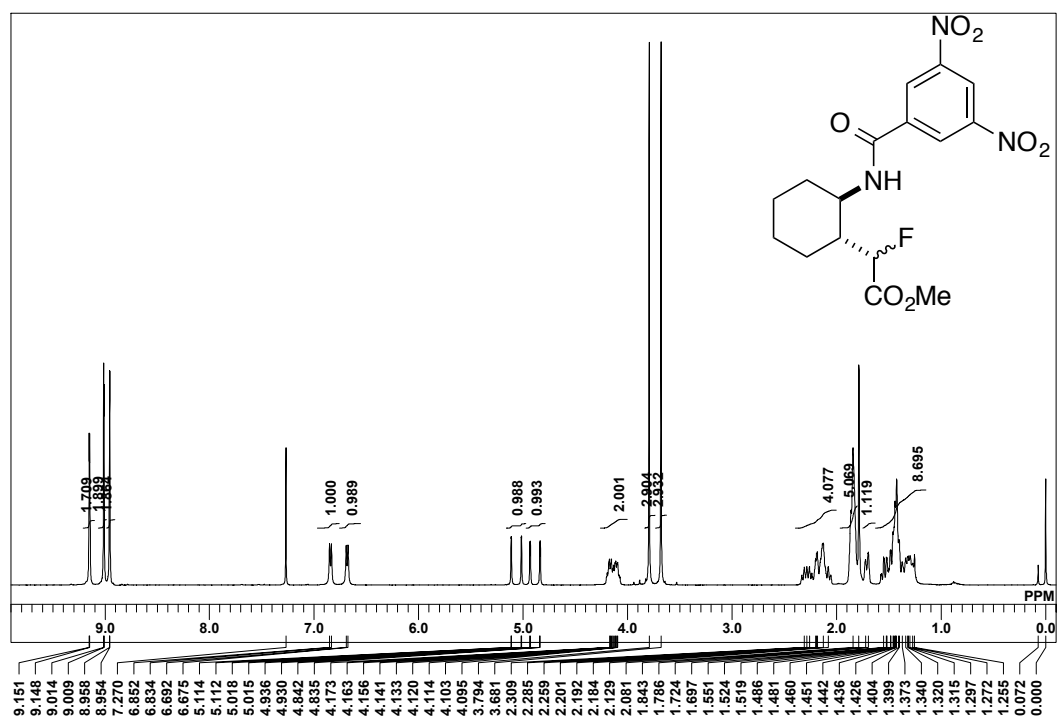


# Dimethyl

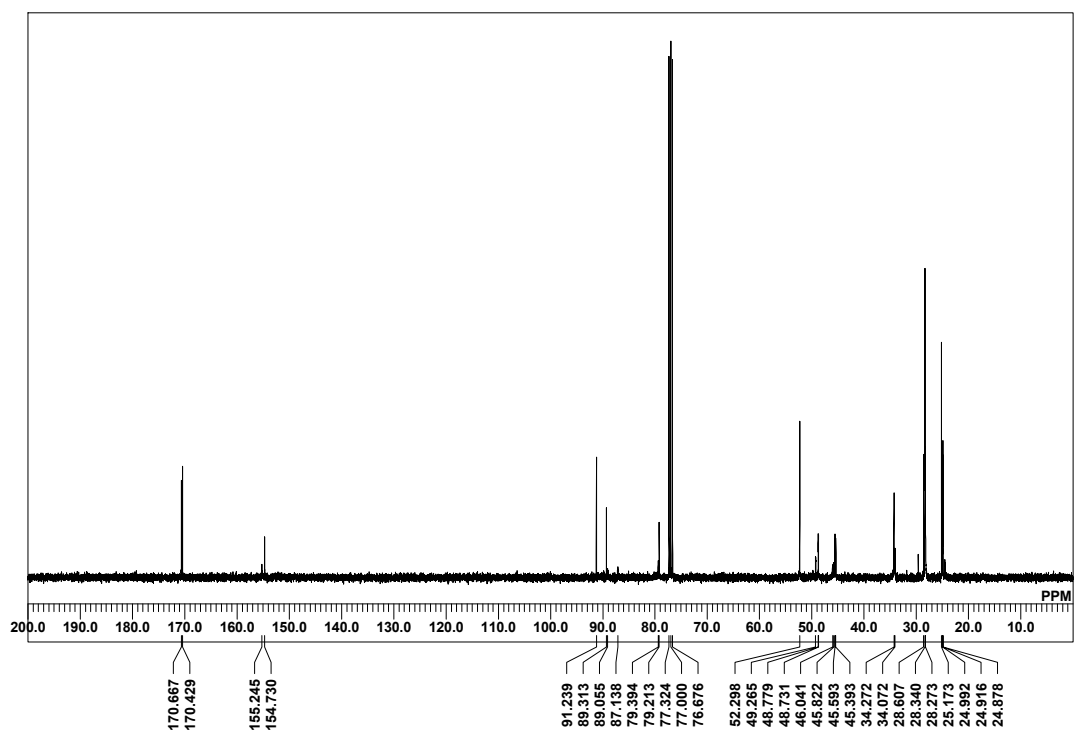
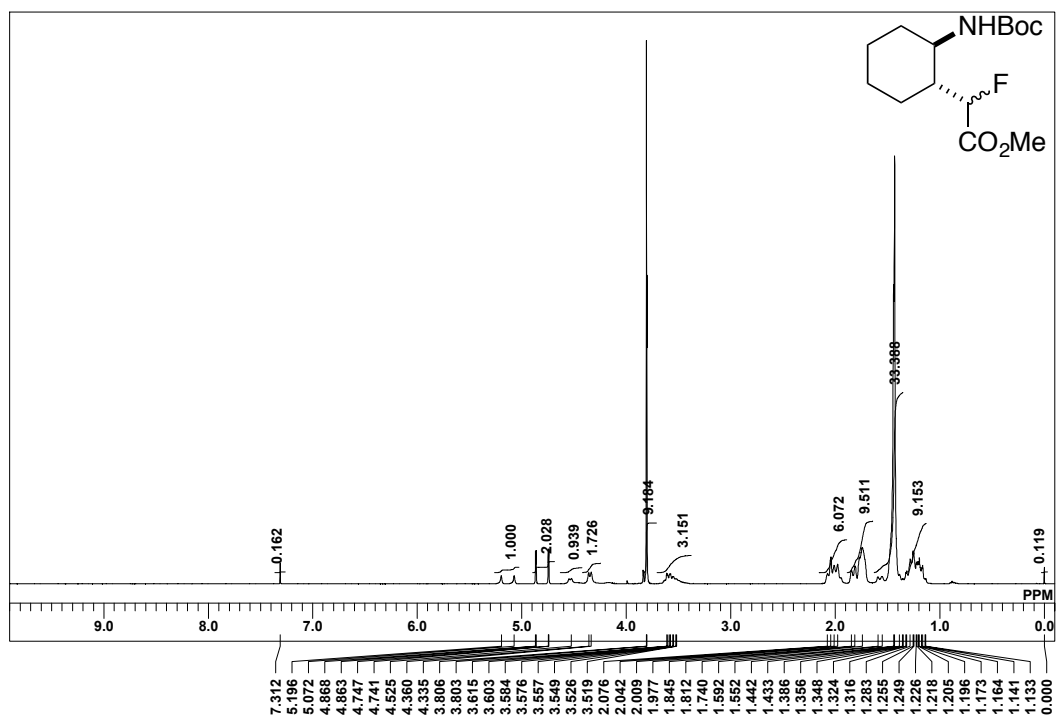
## 2-((1*R*,6*R*)-6-(3,5-dinitrobenzamido)cyclohex-3-en-1-yl)-2-fluoromalonate (4fa)



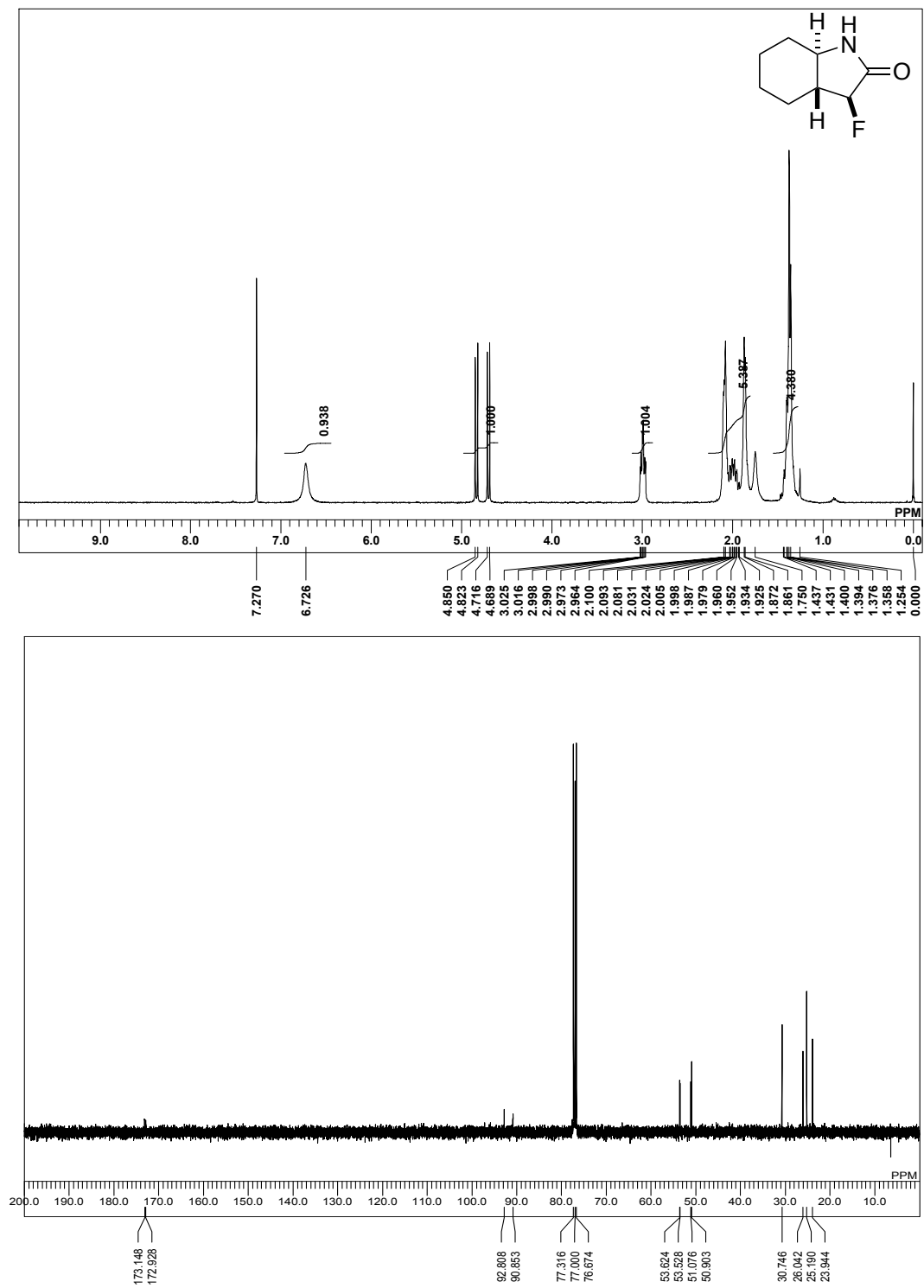
Methyl 2-((1*S*,2*R*)-2-(3,5-dinitrobenzamido)cyclohexyl)-2-fluoroacetate (7aa)



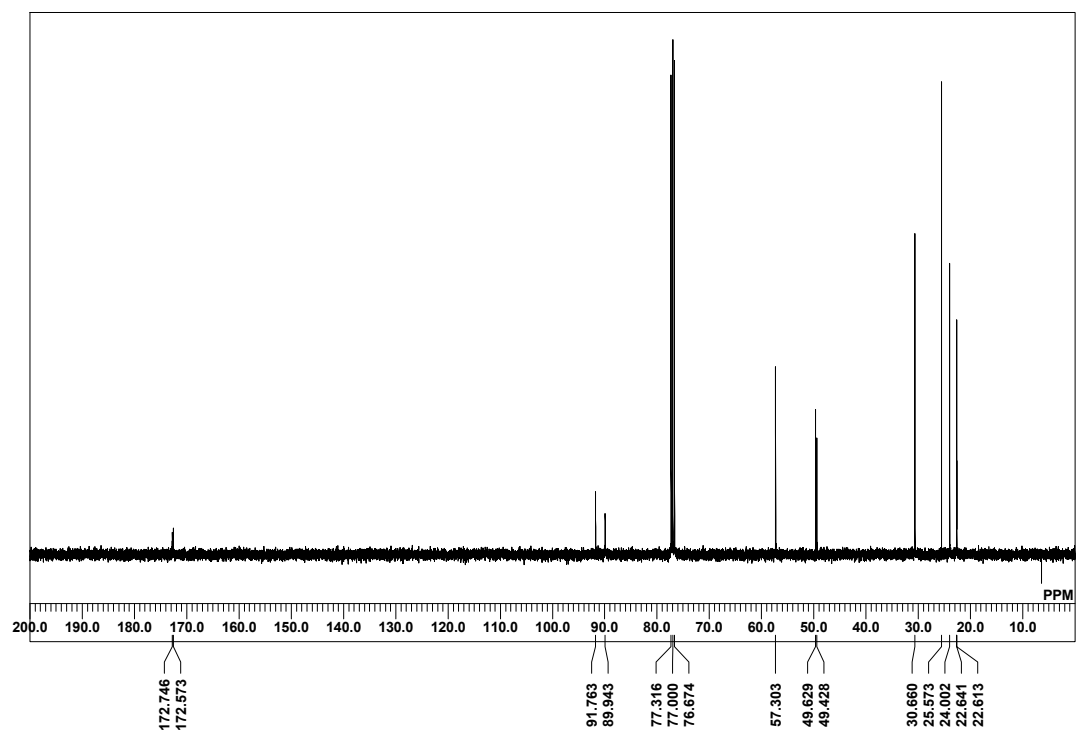
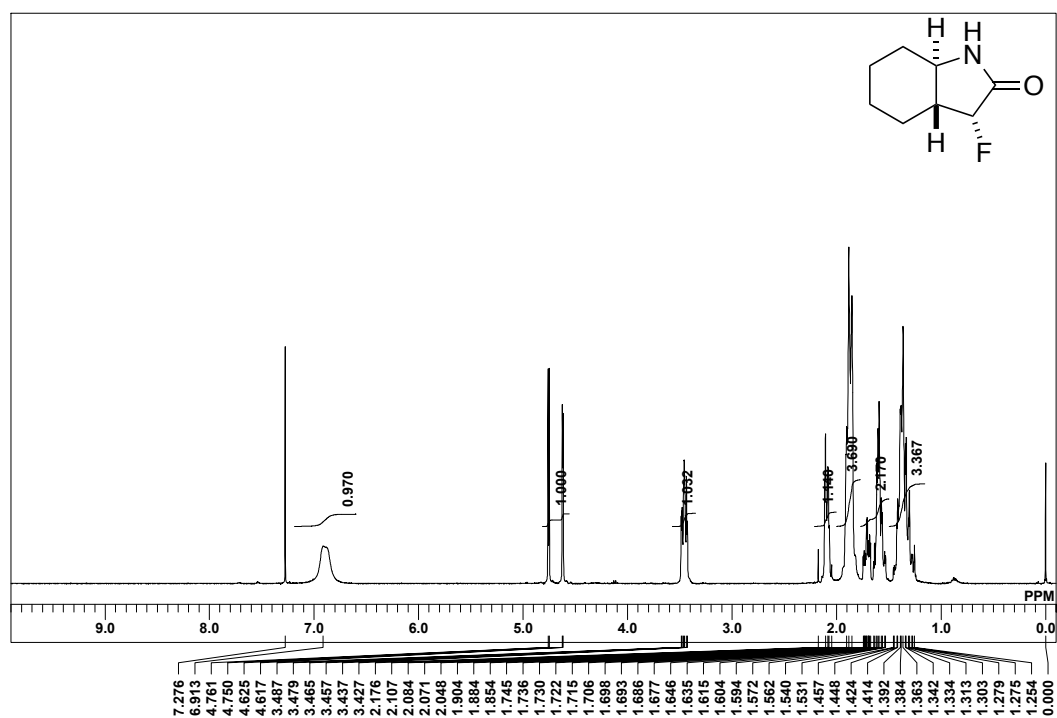
Methyl 2-((1*S*,2*R*)-2-(*tert*-butoxycarbonylamino)cyclohexyl)-2-fluoroacetate (**8aa**)

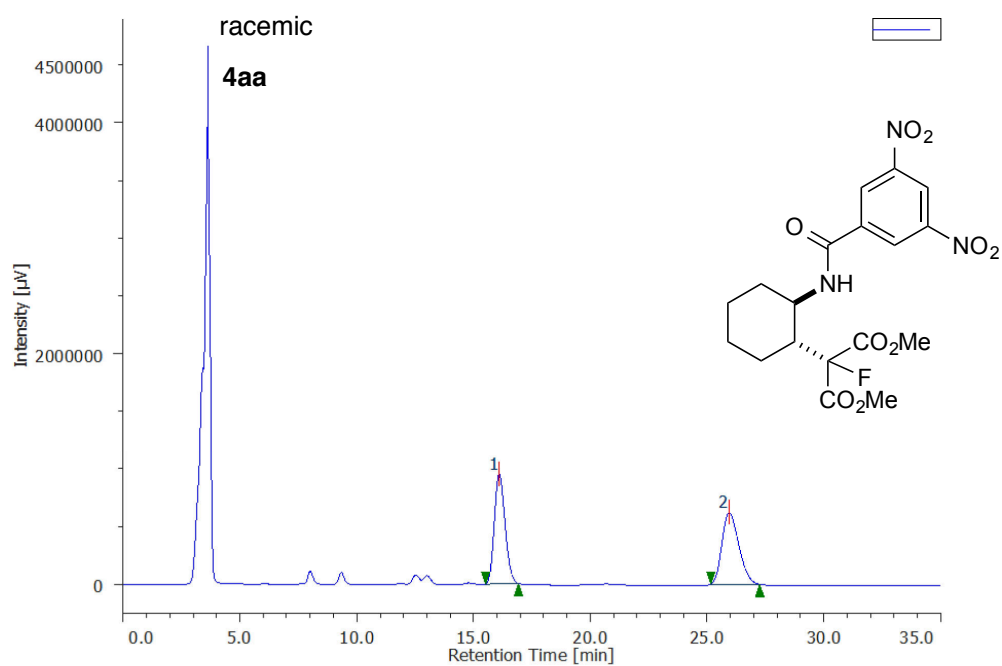


(3*S*, 3*aR*, 7*aR*)-3-fluorooctahydro-2*H*-indol-2-one (10aa)

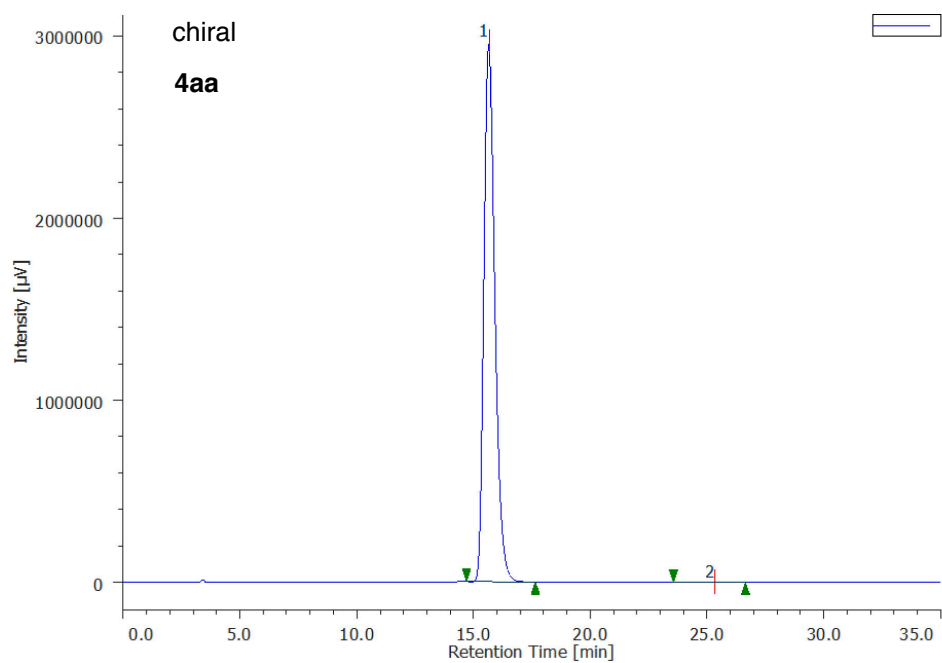


(3*R*, 3*aR*, 7*aR*)-3-fluorooctahydro-2*H*-indol-2-one (10'aa)

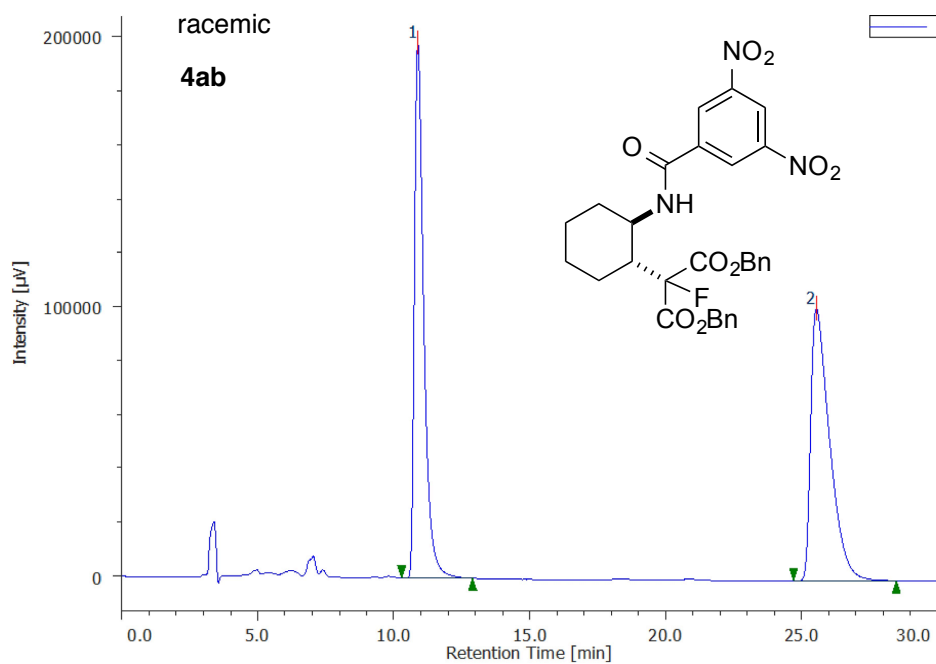




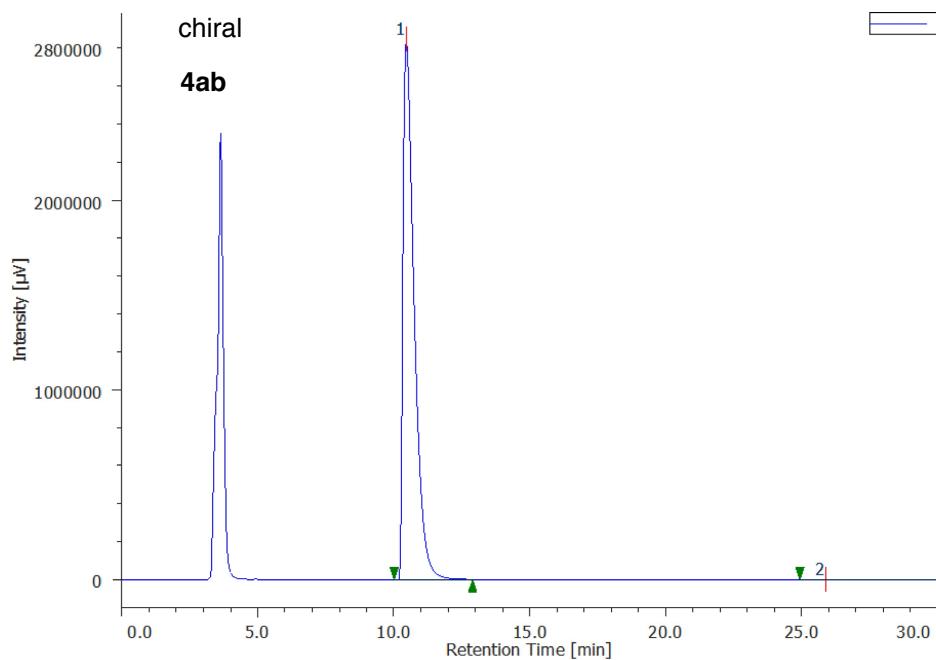
#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	9	16.090	30154583	947902	49.381	60.557	N/A	5783	9.046	1.180	
2	Unknown	9	25.940	30910211	617391	50.619	39.443	N/A	6022	N/A	1.268	



#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	9	15.667	95070340	2964658	99.866	99.911	N/A	5657	9.115	1.244	
2	Unknown	9	25.340	127874	2641	0.134	0.089	N/A	6126	N/A	1.184	

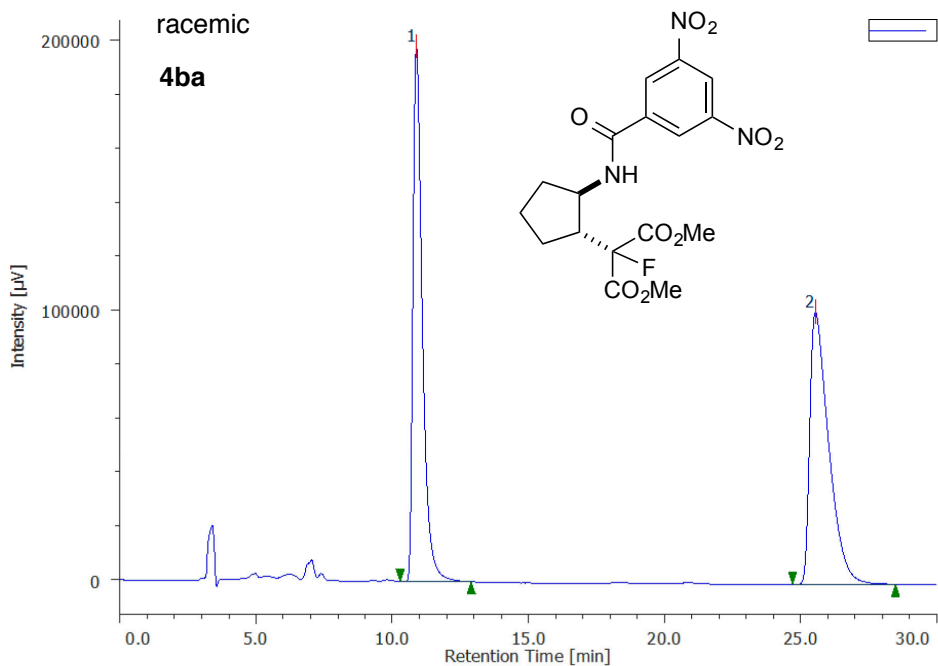


#	ピーク名	CH	tR [min]	面積 [ $\mu\text{V}\cdot\text{sec}$ ]	高さ [ $\mu\text{V}$ ]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	9	10.887	4762920	198203	49.493	66.291	N/A	5257	15.956	1.724	
2	Unknown	9	25.547	4860582	100788	50.507	33.709	N/A	6770	N/A	2.038	

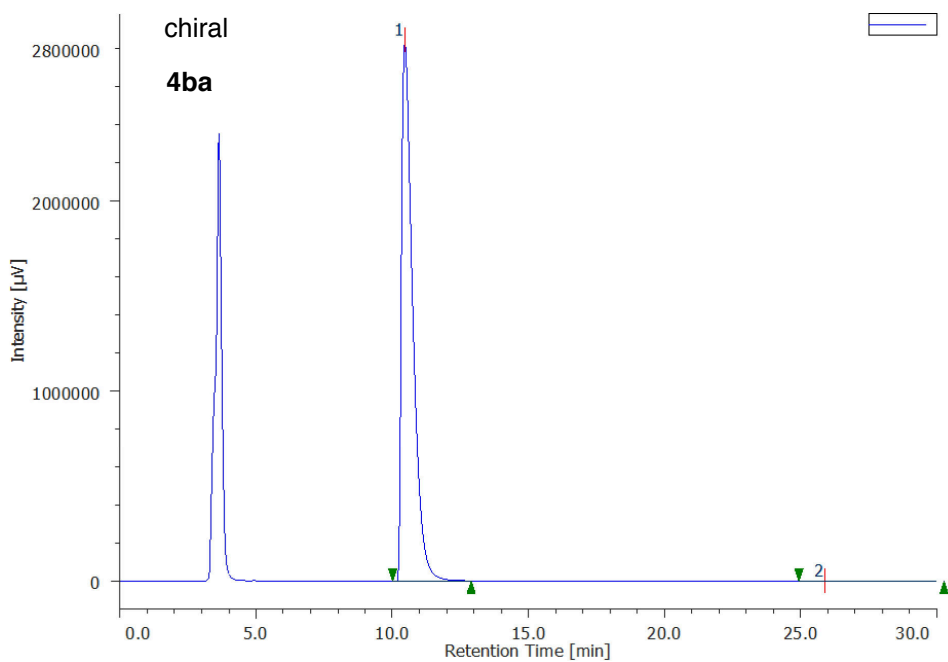


#	ピーク名	CH	tR [min]	面積 [ $\mu\text{V}\cdot\text{sec}$ ]	高さ [ $\mu\text{V}$ ]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	9	10.463	81267991	2841273	99.822	99.911	N/A	3256	14.884	2.236	
2	Unknown	9	25.877	144513	2524	0.178	0.089	N/A	5938	N/A	1.761	

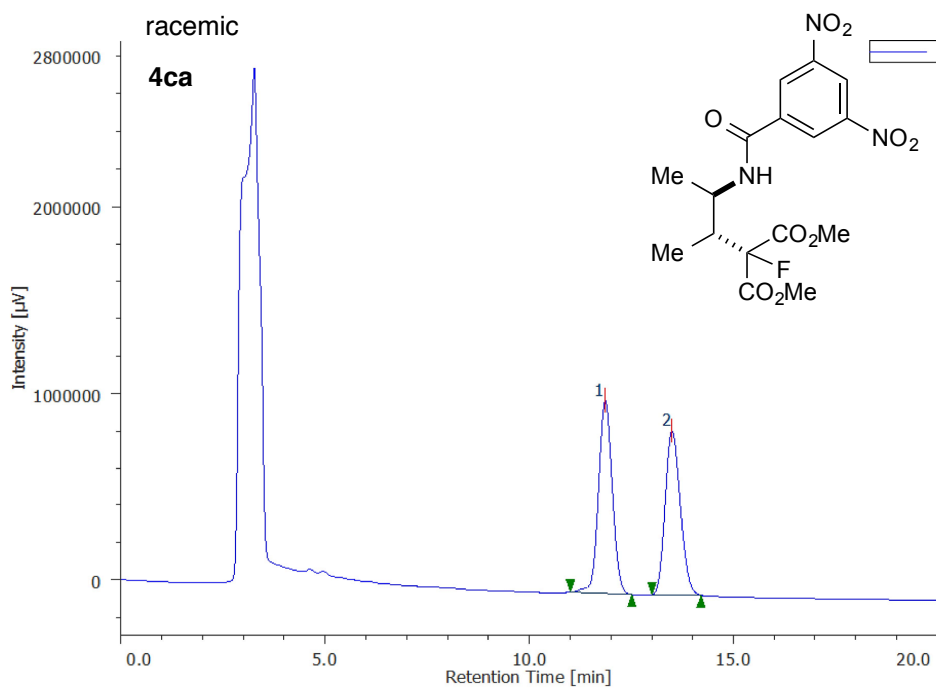




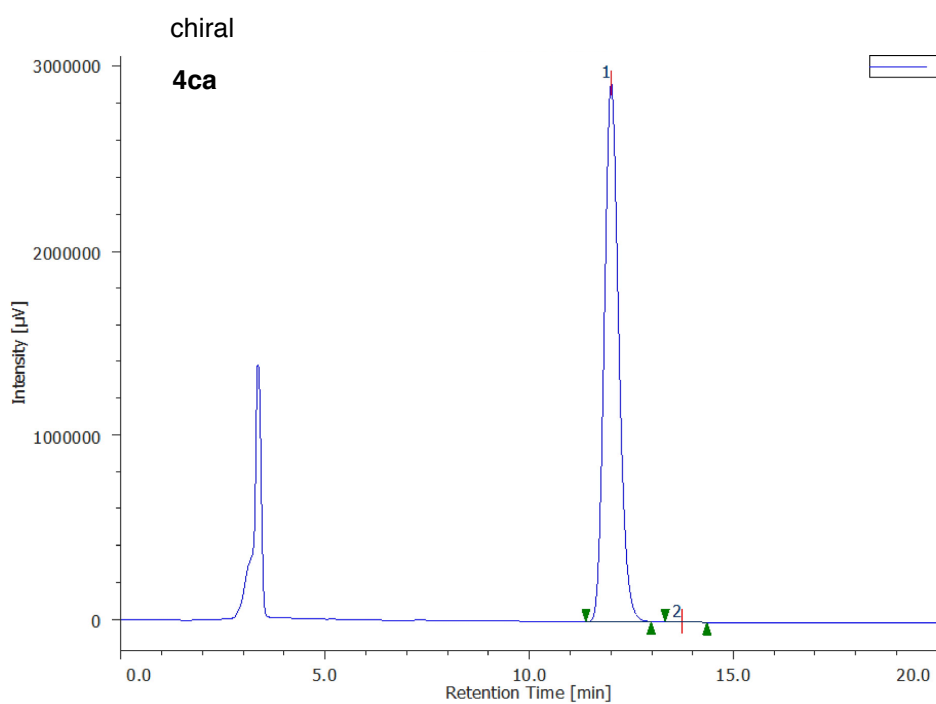
#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シメトリー係数	警告
1	Unknown	9	10.887	4762920	198203	49.493	66.291	N/A	5257	15.956	1.724	
2	Unknown	9	25.547	4860582	100788	50.507	33.709	N/A	6770	N/A	2.038	



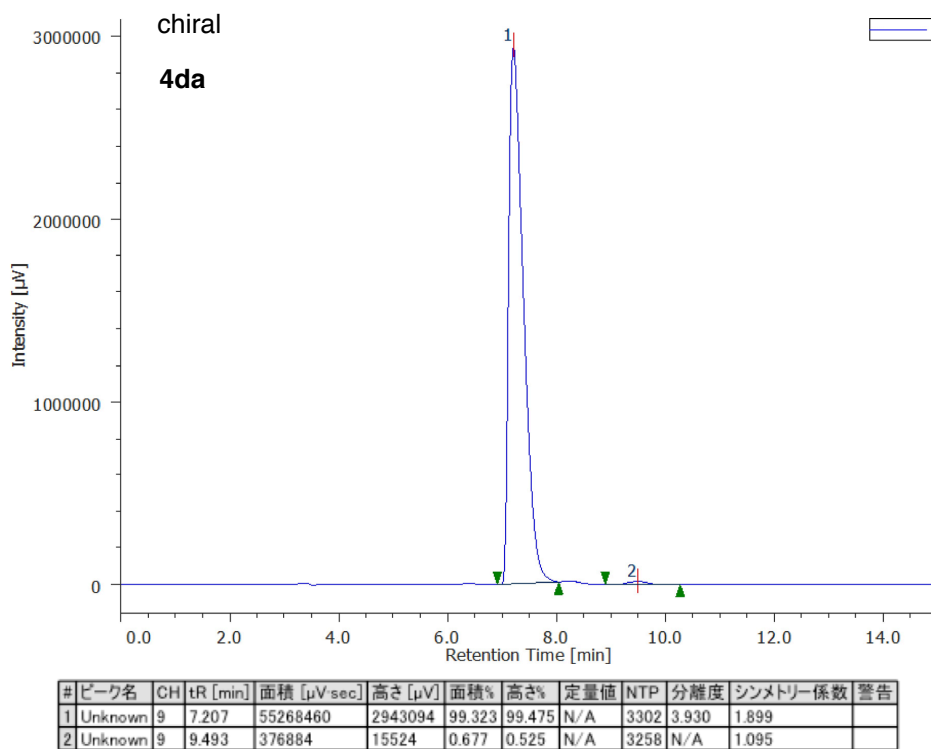
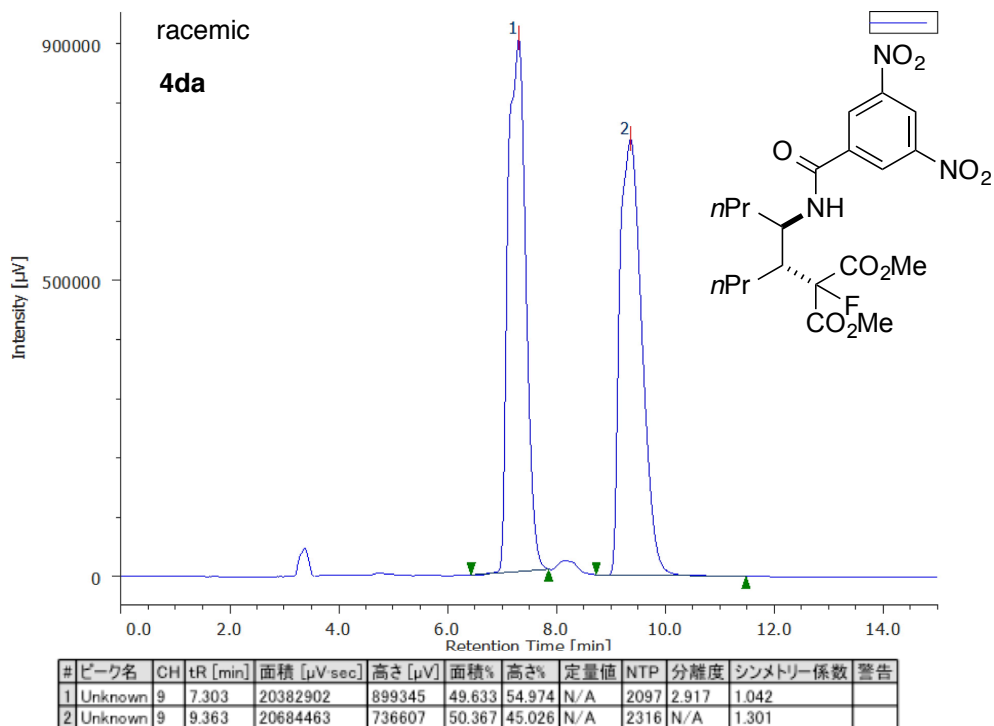
#	ピーク名	CH	tR [min]	面積 [μV·sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シメトリー係数	警告
1	Unknown	9	10.463	81267991	2841273	99.822	99.911	N/A	3256	14.884	2.236	
2	Unknown	9	25.877	144513	2524	0.178	0.089	N/A	5938	N/A	1.761	

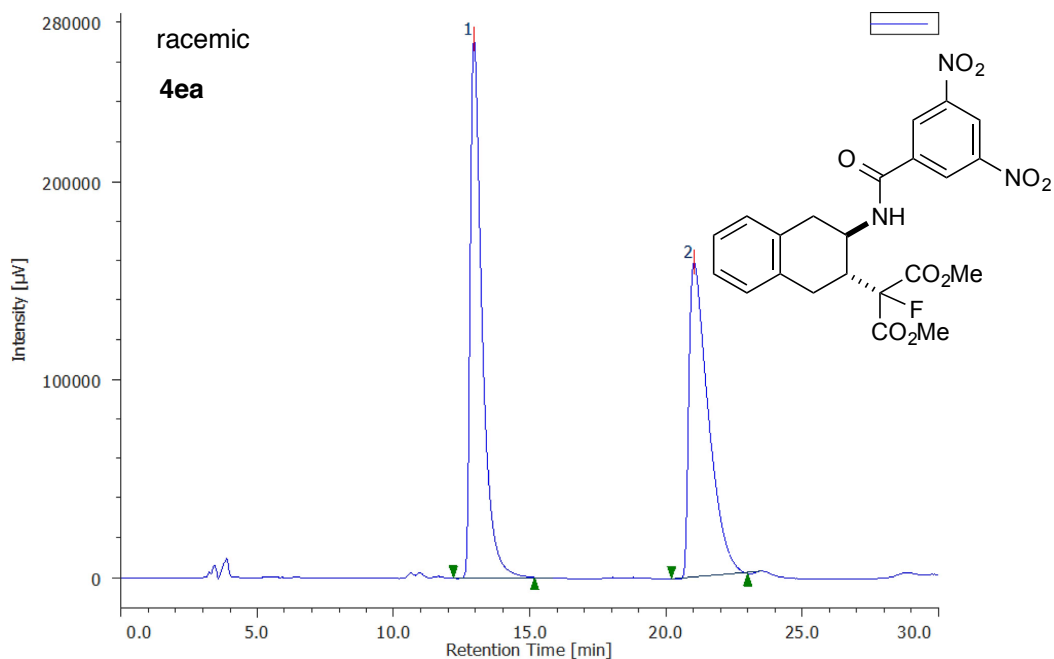


#	ピーク名	CH	tR [min]	面積 [ $\mu\text{V}\cdot\text{sec}$ ]	高さ [ $\mu\text{V}$ ]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	9	11.860	24206789	1033780	51.783	53.955	N/A	6035	2.552	1.059	
2	Unknown	9	13.500	22539431	882225	48.217	46.045	N/A	6344	N/A	1.155	

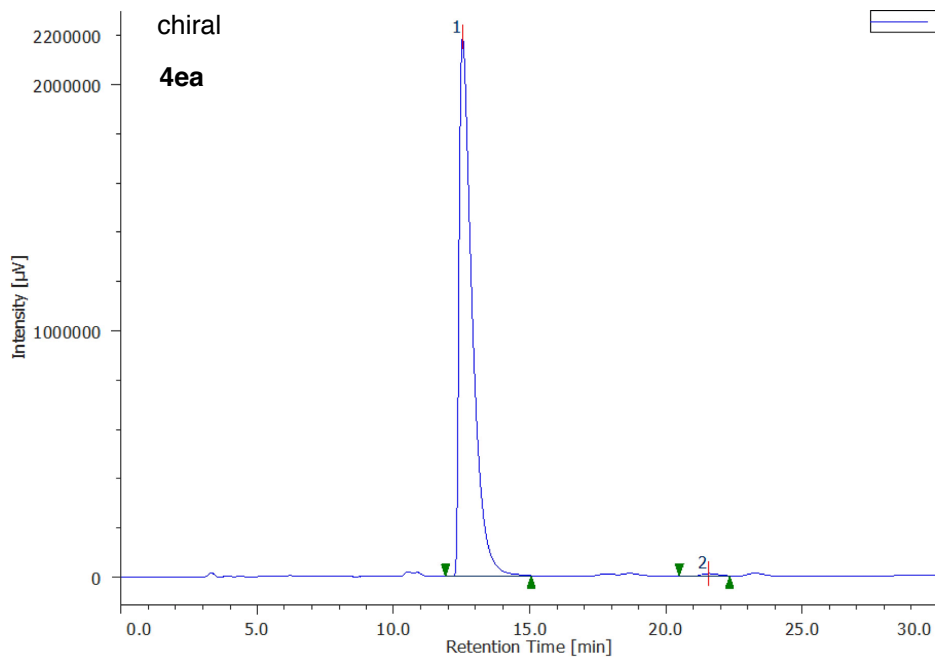


#	ピーク名	CH	tR [min]	面積 [ $\mu\text{V}\cdot\text{sec}$ ]	高さ [ $\mu\text{V}$ ]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	9	12.013	71892841	2920564	99.894	99.900	N/A	5567	2.569	1.133	
2	Unknown	9	13.743	75937	2930	0.106	0.100	N/A	6053	N/A	1.245	

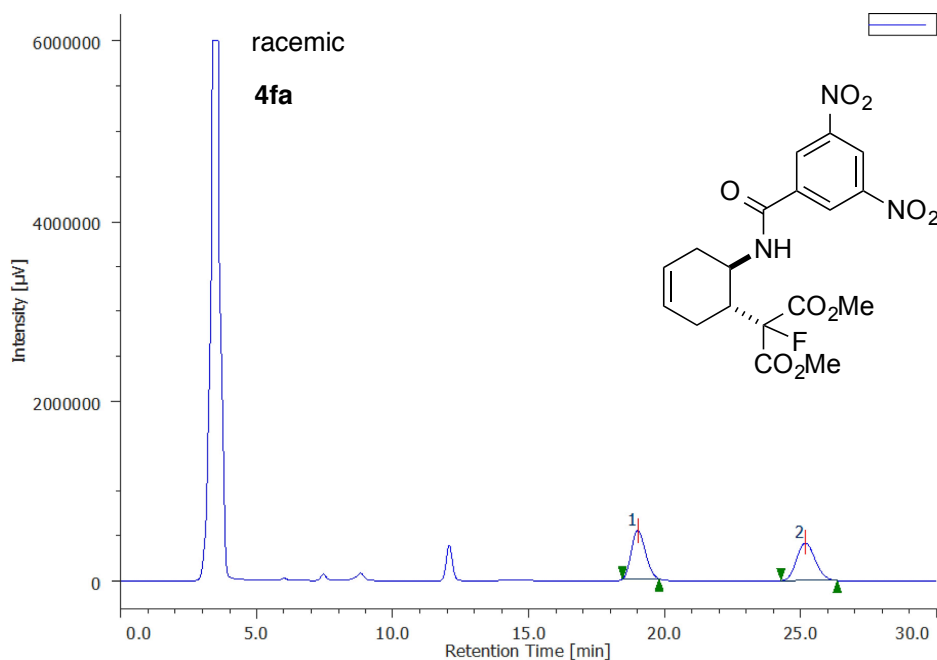




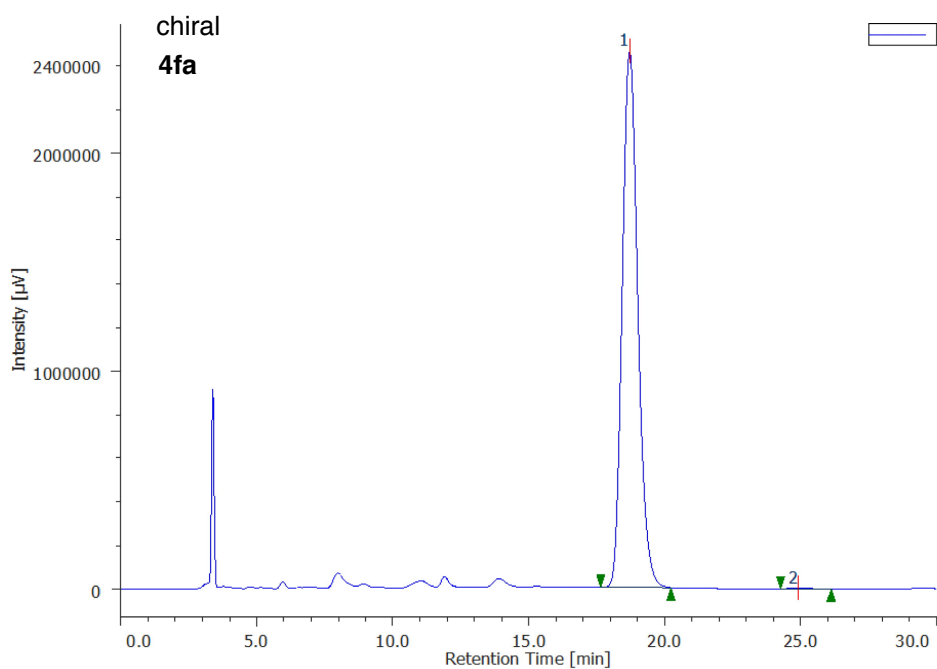
#	ピーク名	CH	tR [min]	面積 [ $\mu\text{V}\cdot\text{sec}$ ]	高さ [ $\mu\text{V}$ ]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	9	12.953	8218269	271179	51.328	63.107	N/A	4883	8.023	2.080	
2	Unknown	9	21.027	7792994	158533	48.672	36.893	N/A	4342	N/A	2.482	



#	ピーク名	CH	tR [min]	面積 [ $\mu\text{V}\cdot\text{sec}$ ]	高さ [ $\mu\text{V}$ ]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	9	12.543	73013755	2186965	99.426	99.538	N/A	3605	9.033	2.519	
2	Unknown	9	21.560	421686	10149	0.574	0.462	N/A	5471	N/A	1.196	



#	ピーク名	CH	tR [min]	面積 [ $\mu\text{V}\cdot\text{sec}$ ]	高さ [ $\mu\text{V}$ ]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	9	19.010	19187859	532531	49.242	56.313	N/A	6121	5.500	1.170	
2	Unknown	9	25.173	19778482	413128	50.758	43.687	N/A	6233	N/A	1.139	



#	ピーク名	CH	tR [min]	面積 [ $\mu\text{V}\cdot\text{sec}$ ]	高さ [ $\mu\text{V}$ ]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	9	18.707	97881214	2458548	99.797	99.829	N/A	5155	5.365	1.185	
2	Unknown	9	24.930	199417	4206	0.203	0.171	N/A	6032	N/A	1.195	