

Asymmetric Michael addition of α -fluoro- α -nitro esters to nitroolefins: towards synthesis of α -fluoro- α -substituted amino acids

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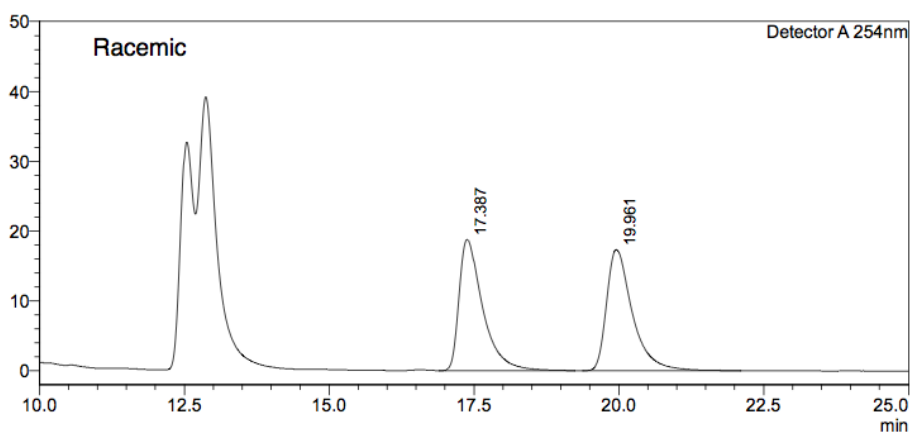
A. HPLC Chromatograms of the Michael Reaction Products

Enantiomeric excesses were successfully assessed for major diastereomers of all products (as shown in table 2 in the article). Attempts were made to assess the ee values for minor diastereomers in cases where dr value was lower than 3:1; however in isolated examples were unsuccessful.

(2S,3S)-Ethyl 2-fluoro-2,4-dinitro-3-phenylbutanoate (3a)

Diastereomers of the chiral product were separated. Initial attempts to resolve the enantiomers of the minor diastereomer on HPLC were unsuccessful and not continued.

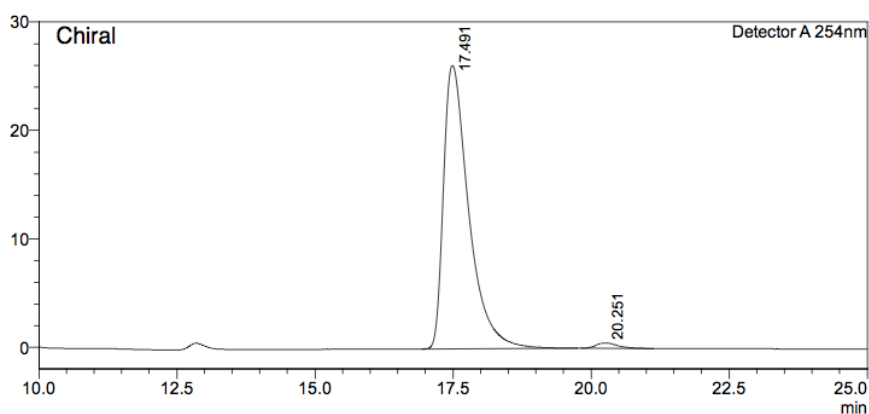
Racemic mixture of diastereomers



<Peak Table>

Detector A 254nm		
Peak#	Ret. Time	Area%
1	17.387	49.811
2	19.961	50.189
Total		100.000

Major diastereomer



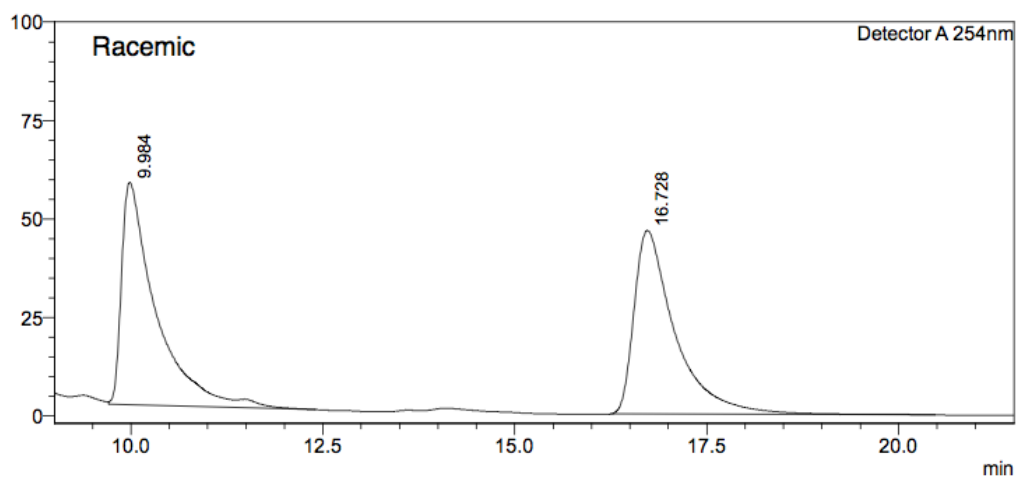
<Peak Table>

Detector A 254nm		
Peak#	Ret. Time	Area%
1	17.491	98.329
2	20.251	1.671
Total		100.000

(2S,3S)-Isopropyl 3-(3-bromophenyl)-2-fluoro-2,4-dinitrobutanoate (3b)

Diastereomers of the chiral and racemic products were separated. Initial attempts to resolve the enantiomers of the minor diastereomer on HPLC were unsuccessful and not continued.

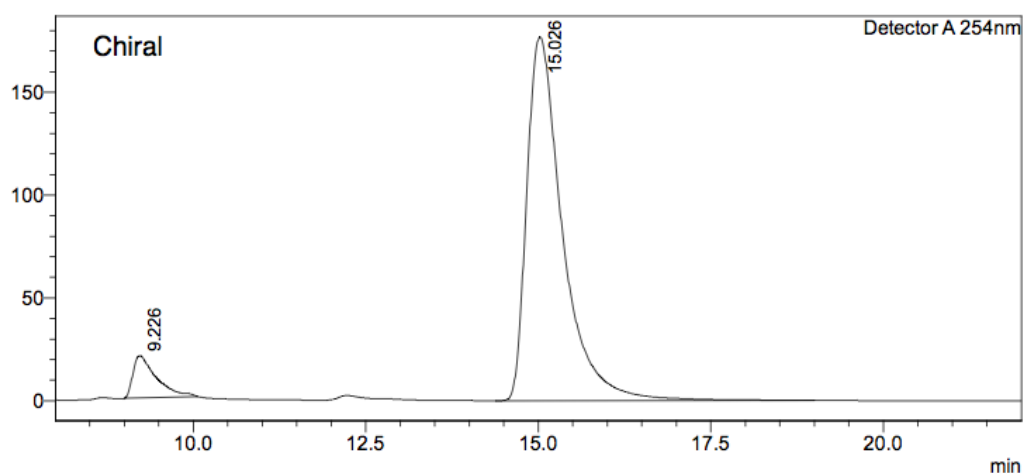
Major diastereomer, racemate (3b)



<Peak Table>

Detector A 254nm		
Peak#	Ret. Time	Area%
1	9.984	50.301
2	16.728	49.699
Total		100.000

Major diastereomer, chiral (3b)



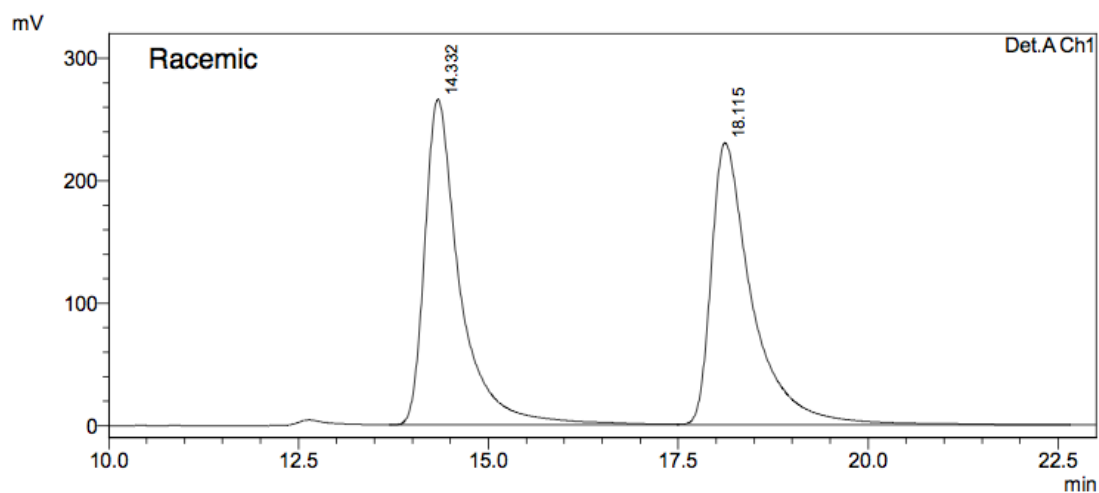
<Peak Table>

Detector A 254nm		
Peak#	Ret. Time	Area%
1	9.226	7.065
2	15.026	92.935
Total		100.000

(2S,3S)-Ethyl 2-fluoro-3-(naphthalen-2-yl)-2,4-dinitrobutanoate (3c)

Diastereomers of the chiral and racemic products were separated. Initial attempts to resolve the enantiomers of the minor diastereomer on HPLC were unsuccessful and not continued.

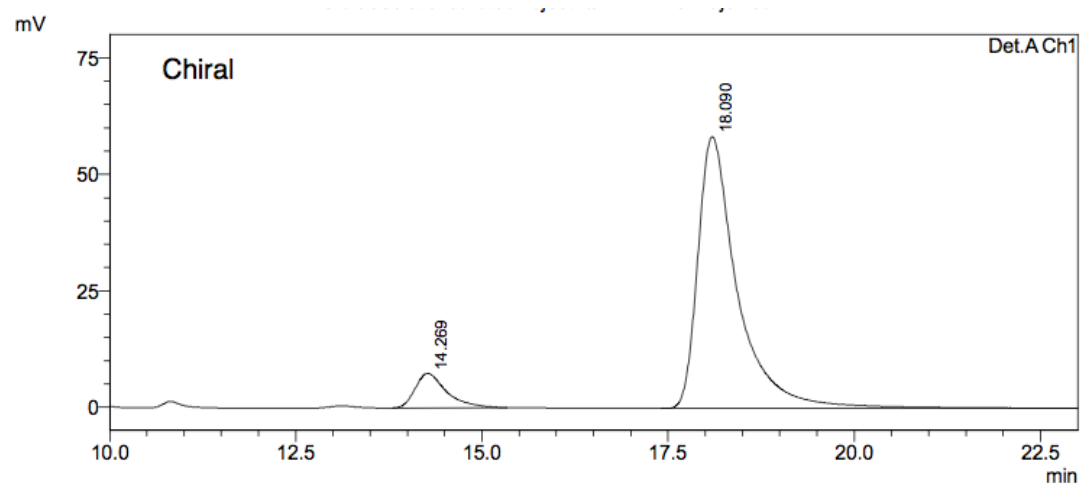
Major diastereomer, racemate (3c)



PeakTable

Detector A Ch1 254nm			
Peak#	Ret. Time	Area	Area %
1	14.332	8621081	49.818
2	18.115	8684180	50.182
Total		17305261	100.000

Major diastereomer, chiral (3c)



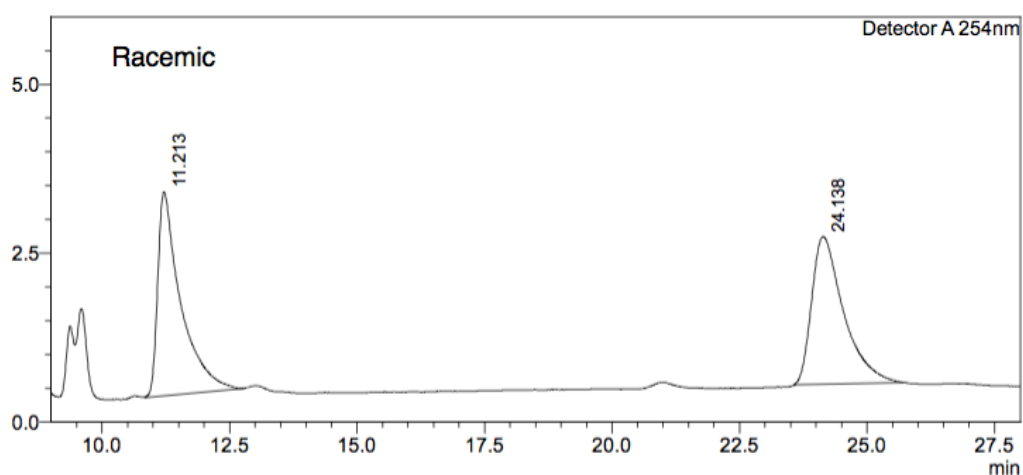
PeakTable

Detector A Ch1 254nm			
Peak#	Ret. Time	Area	Area %
1	14.269	217393	9.066
2	18.090	2180506	90.934
Total		2397899	100.000

(2S,3S)-Ethyl 2-fluoro-2,4-dinitro-3-(4-(trifluoromethyl)phenyl)butanoate (3d)

Diastereomers of the chiral product were separated. Initial attempts to resolve the enantiomers of the minor diastereomer on HPLC were unsuccessful and not continued.

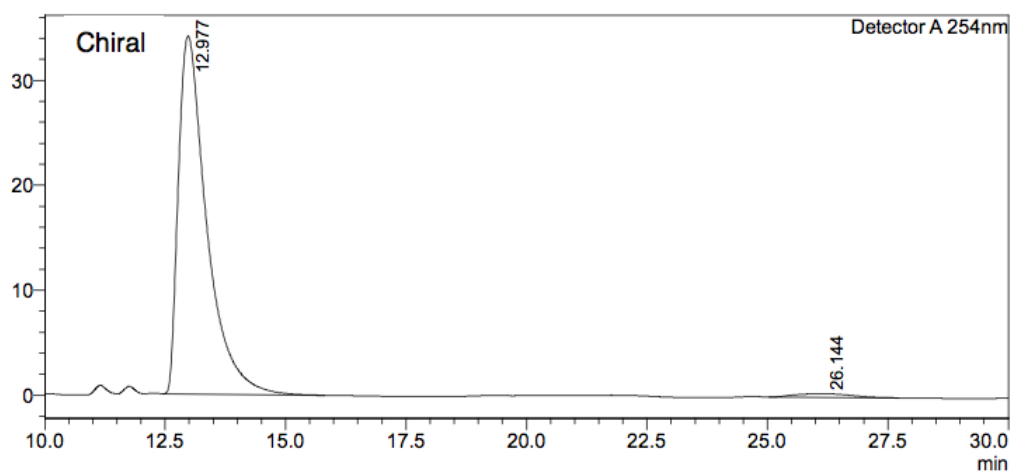
Racemic mixture of diastereomers



<Peak Table>

Detector A 254nm		
Peak#	Ret. Time	Area%
1	11.213	49.905
2	24.138	50.095
Total		100.000

Major diastereomer ((2S,3S), (3d))



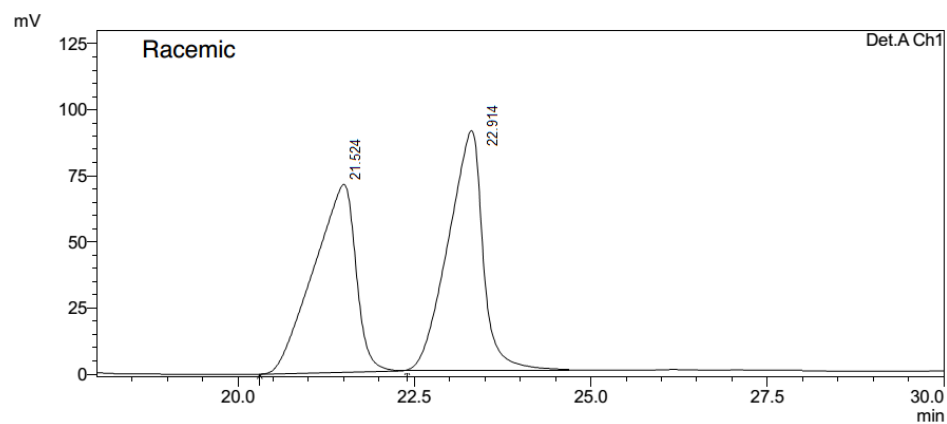
<Peak Table>

Detector A 254nm		
Peak#	Ret. Time	Area%
1	12.977	98.012
2	26.144	1.988
Total		100.000

(2S,3S)-Ethyl 2-fluoro-2,4-dinitro-3-(*p*-tolyl)butanoate (**3e**)

Diastereomers of the chiral and racemic products were separated. Initial attempts to resolve the enantiomers of the minor diastereomer on HPLC were unsuccessful and not continued.

Major diastereomer, racemate (**3e**)

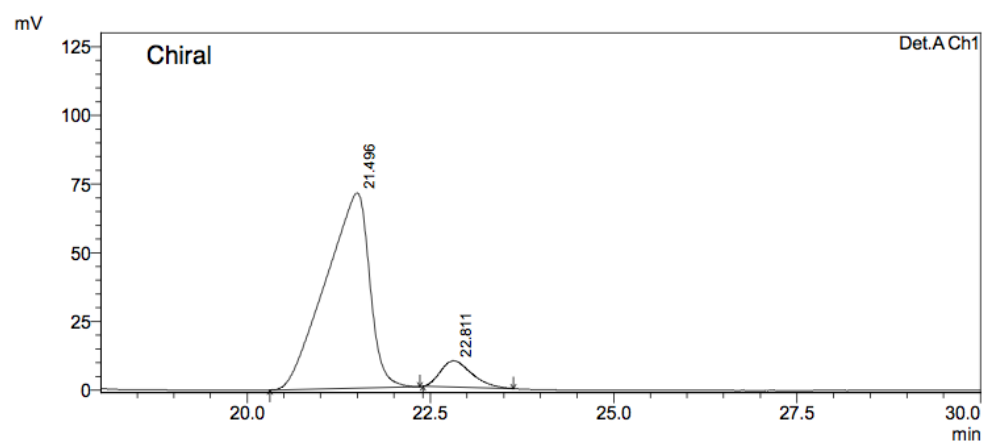


1 Det.A Ch1/254nm

PeakTable
Detector A Ch1 254nm

Peak#	Ret. Time	Area %
1	21.524	49.956
2	22.914	50.044
Total		100.000

Major diastereomer, chiral (**3e**)



1 Det.A Ch1/254nm

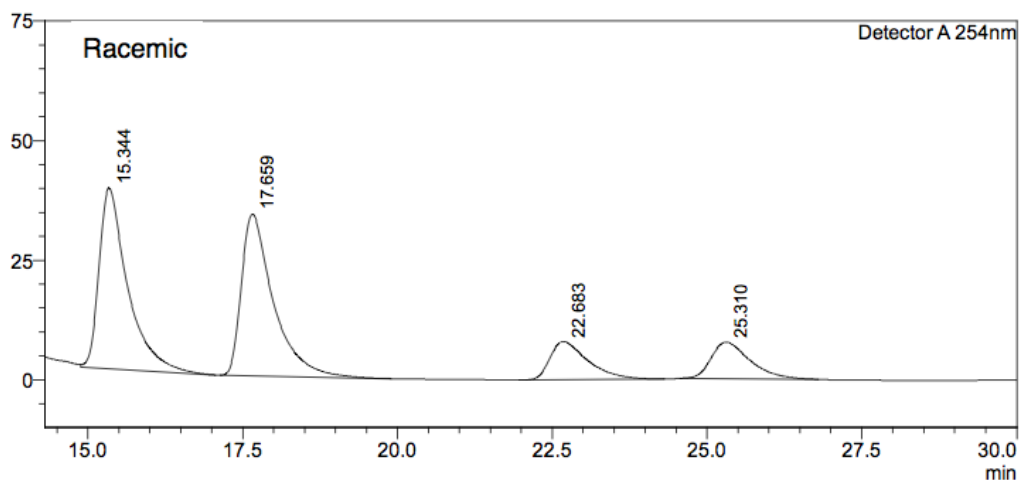
PeakTable
Detector A Ch1 254nm

Peak#	Ret. Time	Area %
1	21.496	91.250
2	22.811	8.750
Total		100.000

(2S,3S)-Ethyl 3-(3-bromophenyl)-2-fluoro-2,4-dinitrobutanoate (3f)

Diastereomers of the chiral product were separated.

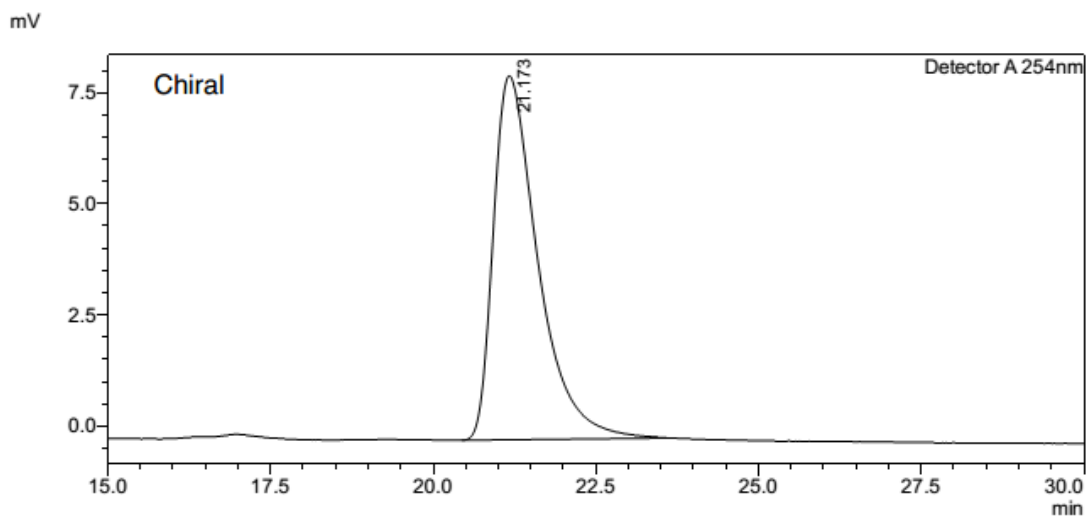
Racemic mixture of diastereomers



<Peak Table>

Detector A 254nm		
Peak#	Ret. Time	Area%
1	15.344	39.119
2	17.659	39.140
3	22.683	10.931
4	25.310	10.810
Total		100.000

Major diastereomer ((2S,3S), 3f)



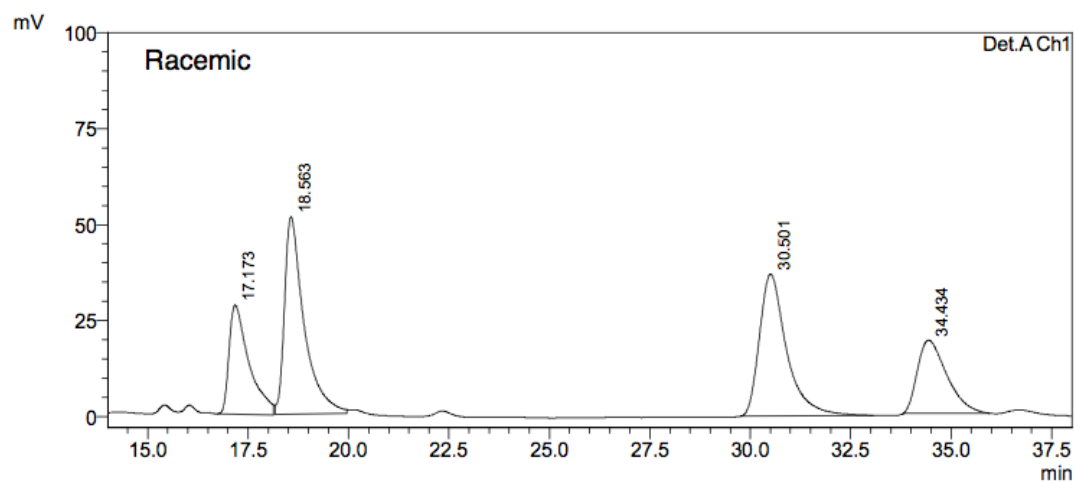
<Peak Table>

Detector A 254nm		
Peak#	Ret. Time	Area%
1	21.173	100.000
Total		100.000

(2S,3S)-Ethyl 2-fluoro-3-(2-fluorophenyl)-2,4-dinitrobutanoate (3g)

Diastereomers were separated in the chiral sample. Resolution on HPLC of enantiomers of both diastereomers was achieved.

Racemic mixture of diastereomers



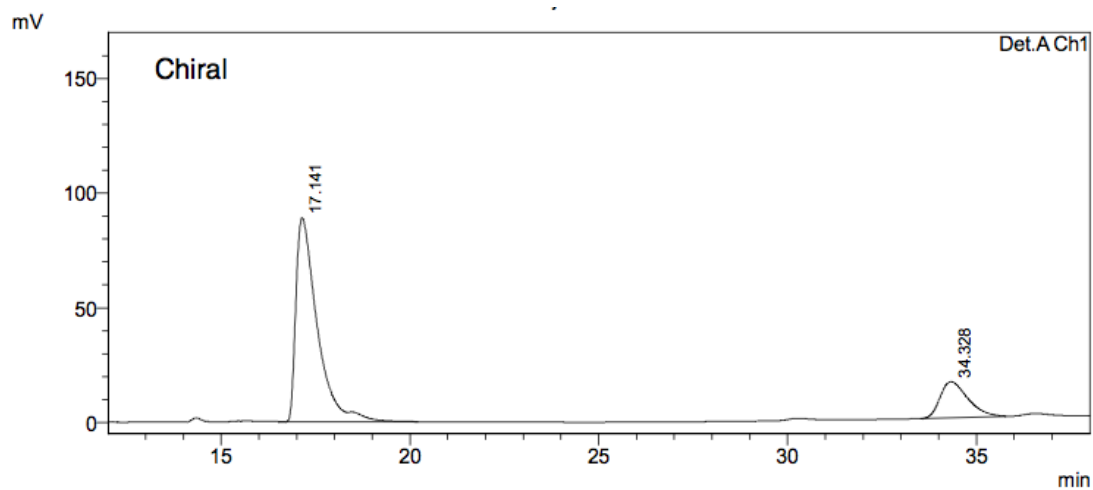
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Area %
1	17.173	977253	18.030
2	18.563	1738428	32.073
3	30.501	1739350	32.090
4	34.434	965143	17.806
Total		5420174	100.000

Major diastereomer (3g)



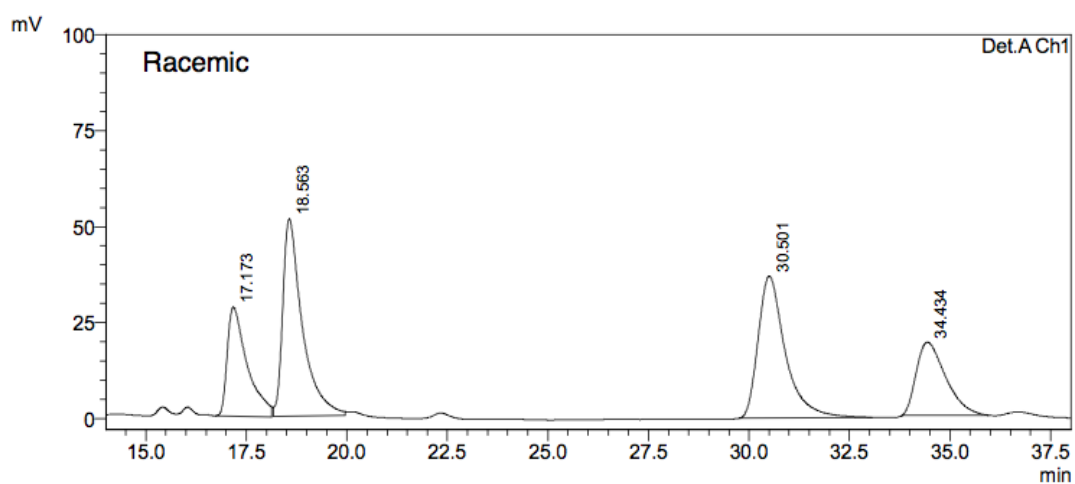
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Area %
1	17.141	3498084	81.405
2	34.328	799028	18.595
Total		4297112	100.000

Racemic mixture of diastereomers

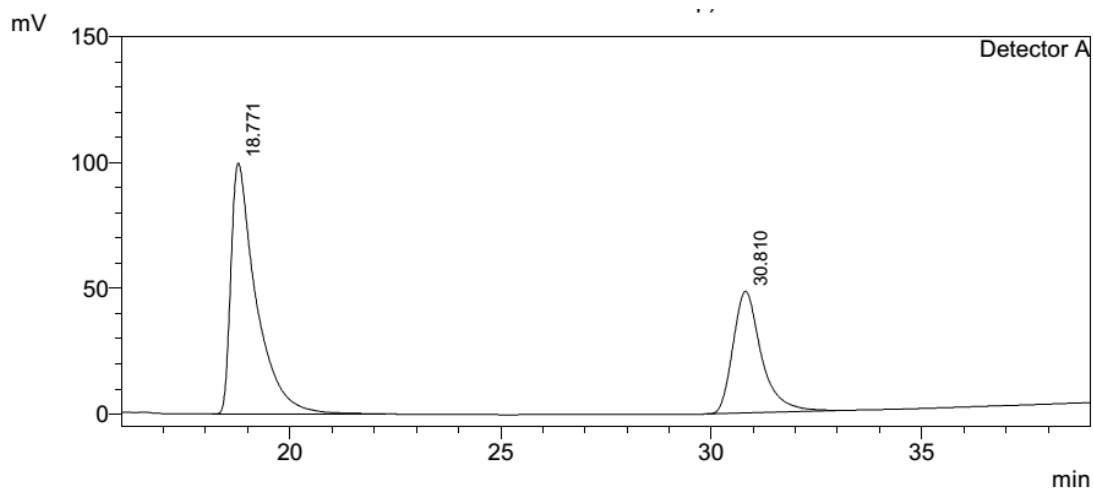


1 Det.A Ch1/254nm

PeakTable

Peak#	Ret. Time	Area	Area %
1	17.173	977253	18.030
2	18.563	1738428	32.073
3	30.501	1739350	32.090
4	34.434	965143	17.806
Total		5420174	100.000

Minor diastereomer (3g')



1 Detector A/254nm

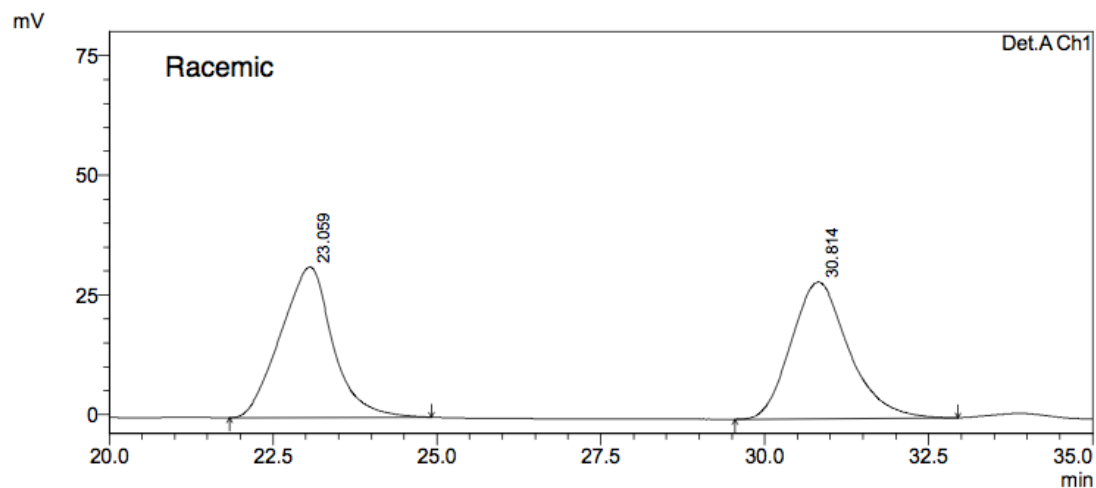
PeakTable

Peak#	Ret. Time	Area	Area %
1	18.771	4148101	64.749
2	30.810	2258300	35.251
Total		6406401	100.000

(2S,3S)-Ethyl 3-(3,4-dichlorophenyl)-2-fluoro-2,4-dinitrobutanoate (3h)

Resolution on HPLC of enantiomers of both diastereomers was achieved. The diastereomers were separated prior to analysis.

Major diastereomer, racemate (3h)



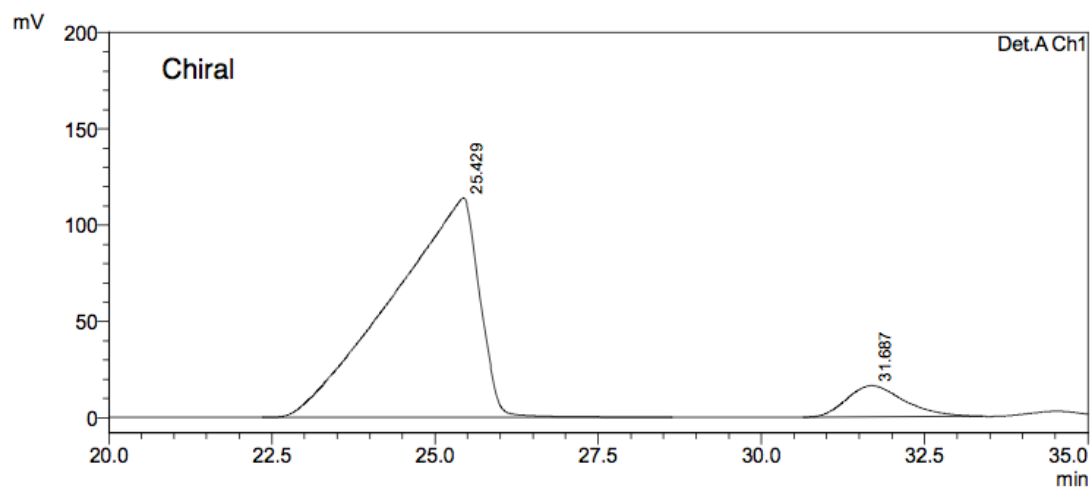
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Area %
1	23.059	1746303	50.027
2	30.814	1744427	49.973
Total		3490730	100.000

Major diastereomer, chiral (3h)



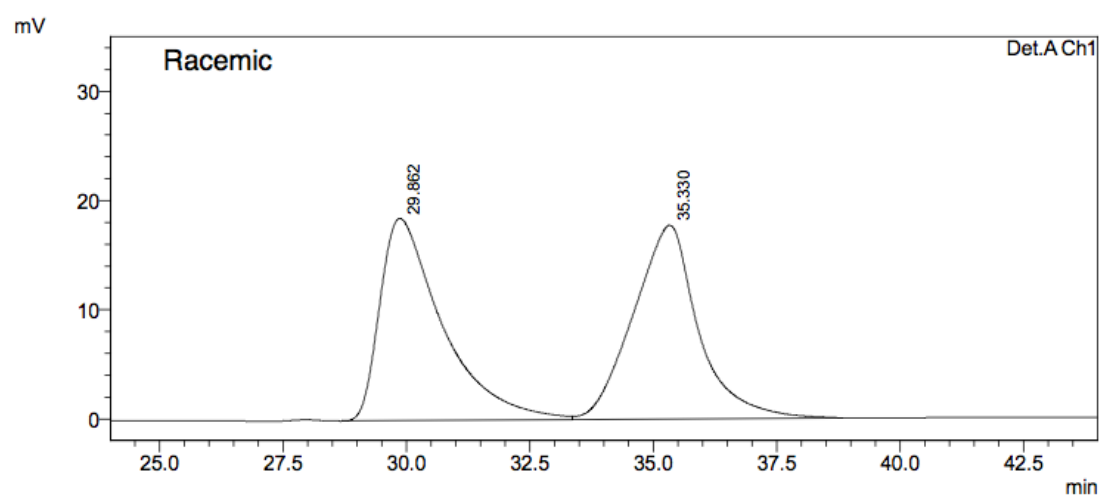
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Area %
1	25.429	10613494	91.393
2	31.687	999594	8.607
Total		11613088	100.000

Minor diastereomer, racemate (3h')



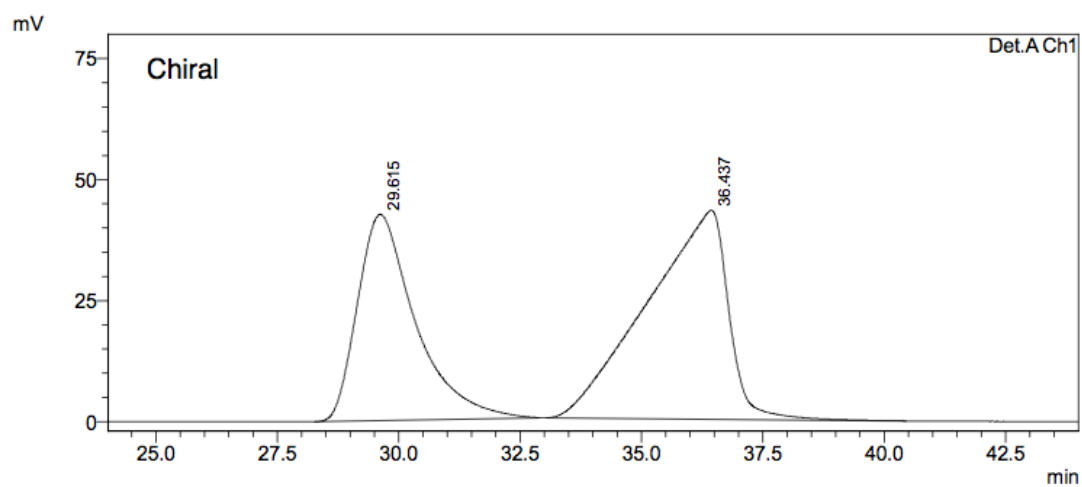
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Area %
1	29.862	1633957	50.052
2	35.330	1630534	49.948
Total		3264490	100.000

Minor diastereomer, chiral (3h')



1 Det.A Ch1/254nm

PeakTable

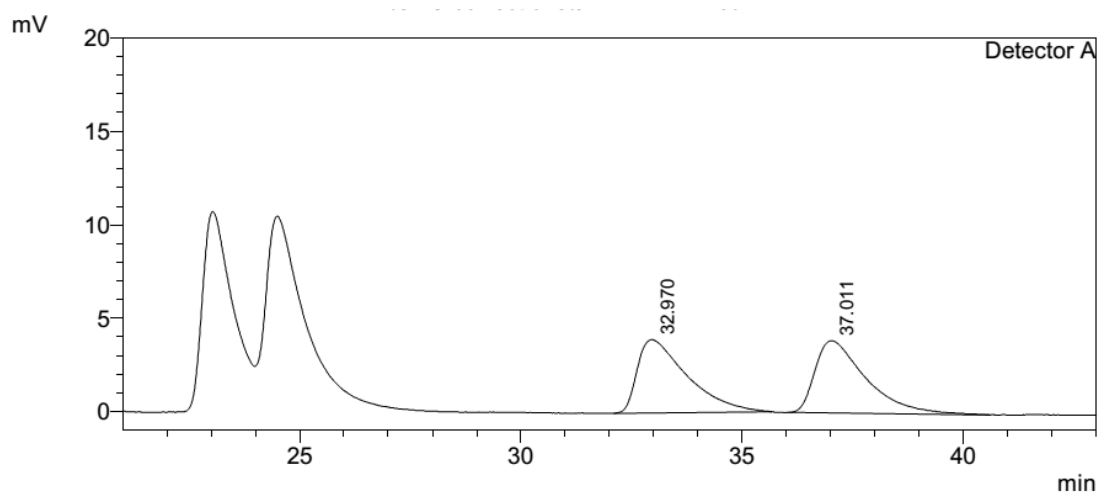
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Area %
1	29.615	3545382	41.289
2	36.437	5041319	58.711
Total		8586700	100.000

(2S,3S)-Ethyl 3-(3,4-dimethoxyphenyl)-2-fluoro-2,4-dinitrobutanoate (3i)

Diastereomers of the chiral and racemic products could not be fully separated. Attempts to resolve the enantiomers of the minor diastereomer on HPLC were unsuccessful. Major diastereomer was identified based on comparison of intensities of light absorption between racemic sample and enantio- and diastereo-enriched sample.

Racemic mixture of diastereomers 3i)



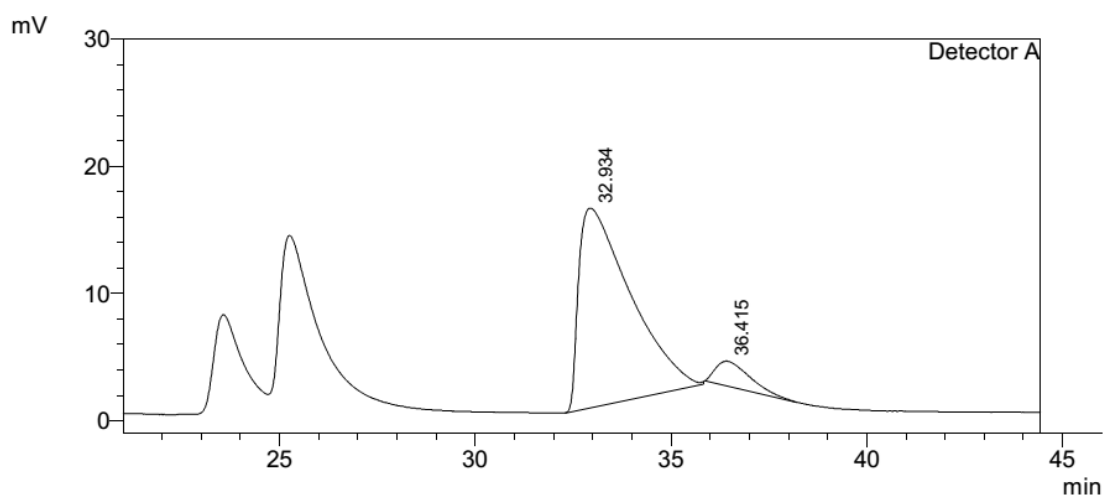
1 Detector A/254nm

PeakTable

Detector A 254nm

Peak#	Ret. Time	Area	Area %
1	32.970	307614	49.902
2	37.011	308825	50.098
Total		616439	100.000

Chiral mixture of diastereomers (3i)



1 Detector A/254nm

PeakTable

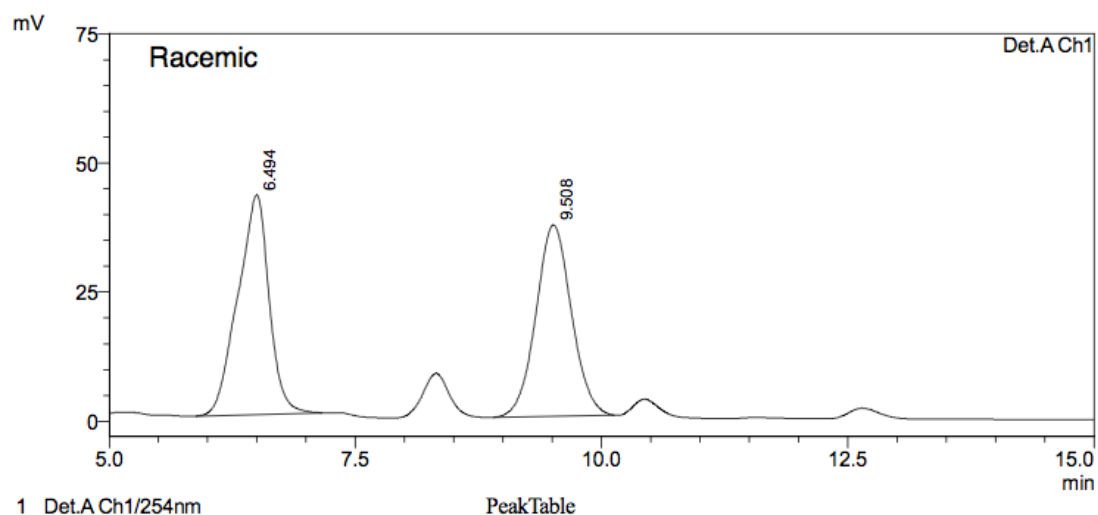
Detector A 254nm

Peak#	Ret. Time	Area	Area %
1	32.934	1436144	92.290
2	36.415	119976	7.710
Total		1556120	100.000

(2S,3S)-Ethyl 3-(3,5-difluorophenyl)-2-fluoro-2,4-dinitrobutanoate (3j)

Diastereomers of the chiral and racemic products were separated. Initial attempts to resolve the enantiomers of the minor diastereomer on HPLC were unsuccessful.

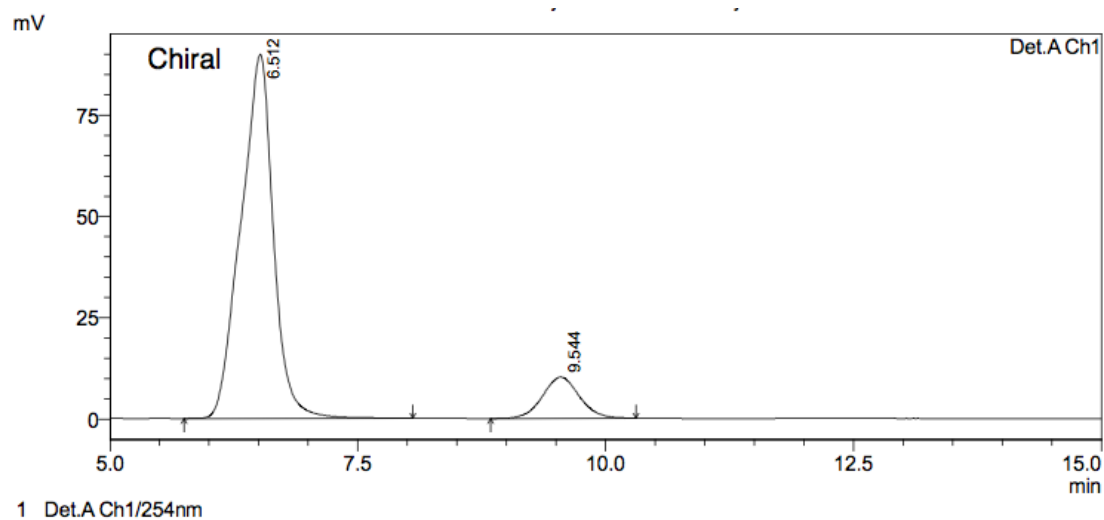
Major diastereomer, racemate (3j)



PeakTable

Peak#	Ret. Time	Area	Area %
1	6.494	941318	50.285
2	9.508	930637	49.715
Total		1871955	100.000

Major diastereomer, chiral (3j)



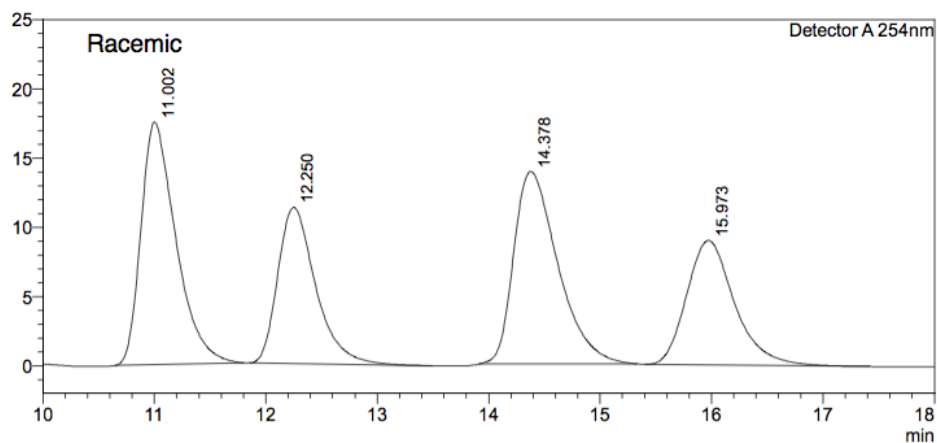
PeakTable

Peak#	Ret. Time	Area	Area %
1	6.512	2047454	88.635
2	9.544	262523	11.365
Total		2309976	100.000

(2S,3R)-Ethyl 2-fluoro-3-(furan-2-yl)-2,4-dinitrobutanoate (3k)

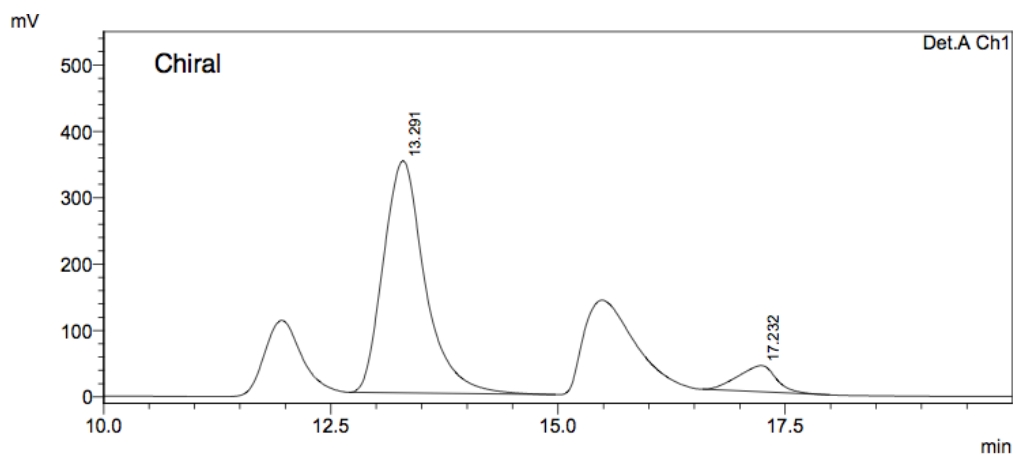
Diastereomers of the chiral and racemic products could not be fully separated. Resolution on HPLC of enantiomers of both diastereomers was achieved.

Mixture of racemic diastereomers (3k)



Peak#	Ret. Time	Area%
1	11.002	29.324
2	12.250	20.551
3	14.378	29.449
4	15.973	20.676
Total		100.000

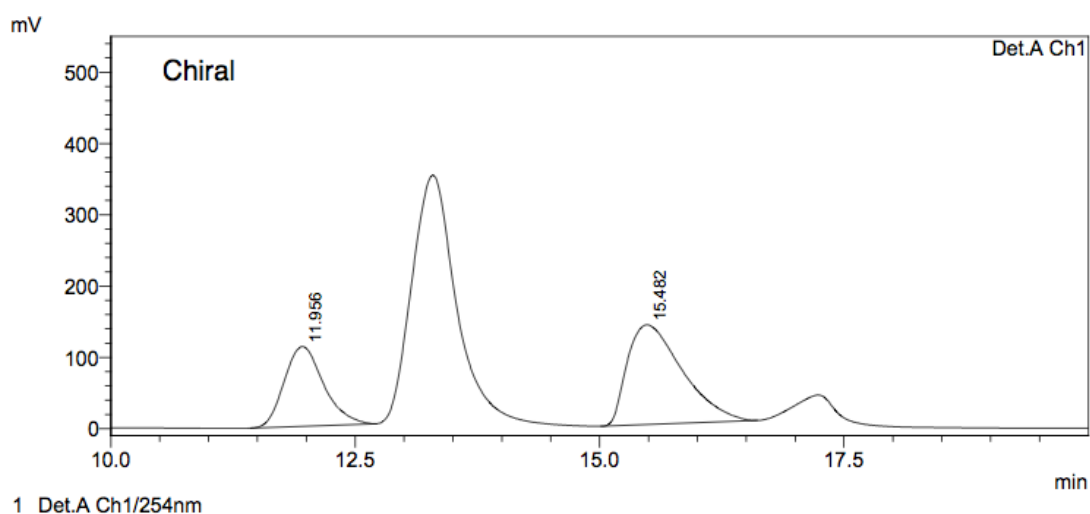
Major diastereomer ((2S,3R), 3k)



1 Det.A Ch1/254nm

PeakTable		
Detector A Ch1 254nm		
Peak#	Ret. Time	Area %
1	13.291	90.598
2	17.232	9.402
Total		100.000

Minor diastereomer ((2R,3R), 3k')



1 Det.A Ch1/254nm

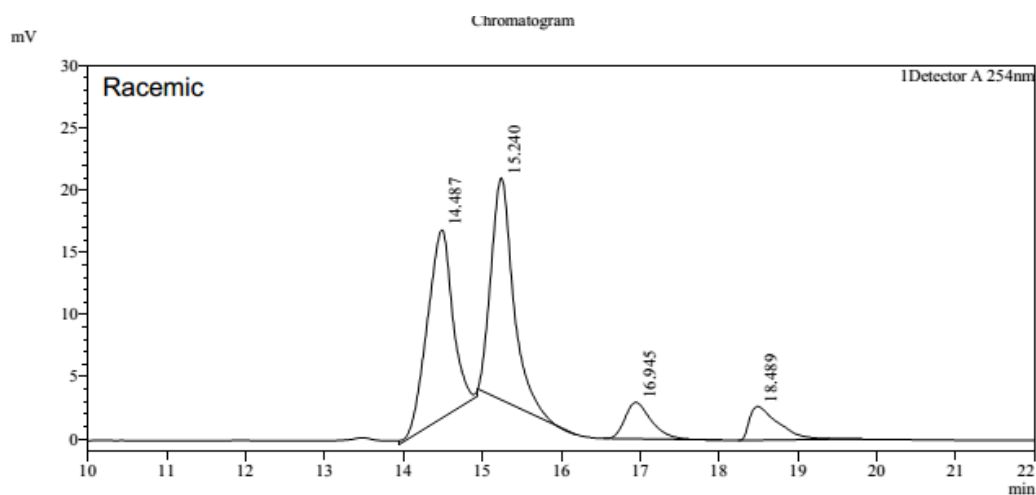
PeakTable
Detector A Ch1 254nm

Peak#	Ret. Time	Area %
1	11.956	36.434
2	15.482	63.566
Total		100.000

(2S,3S)-Ethyl 2-fluoro-2-nitro-3-(nitromethyl)-5-phenylpentanoate (3l)

Diastereomers of the chiral and racemic products were separated. Attempts to resolve the enantiomers of the minor diastereomer on HPLC were partially successful. Enantiomers of the major diastereomer were fully resolved on HPLC.

Racemic, both diastereomers of 3l



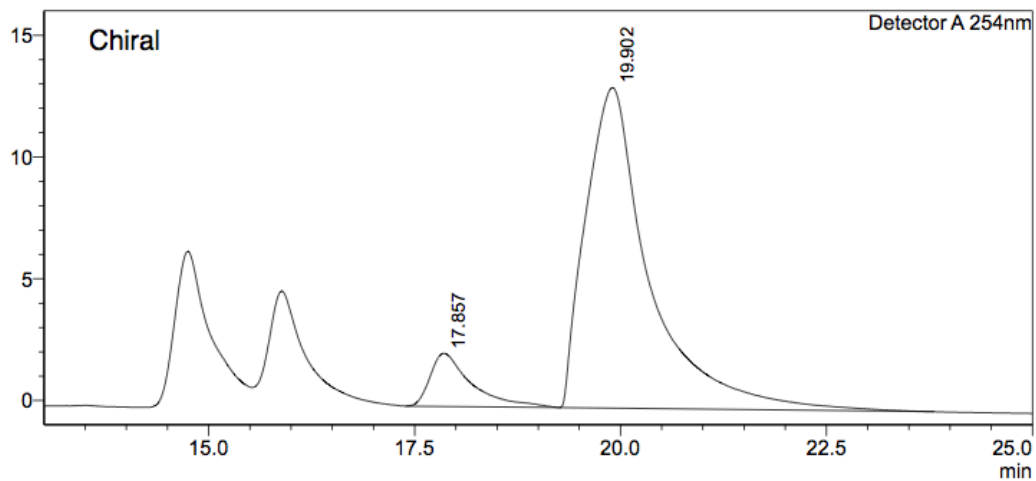
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area%
1	14.487	40.842
2	15.240	42.564
3	16.945	8.288
4	18.489	8.307
Total		100.000

Diastereomeric mixture of the chiral sample (3I), prior to separation of diastereomers.

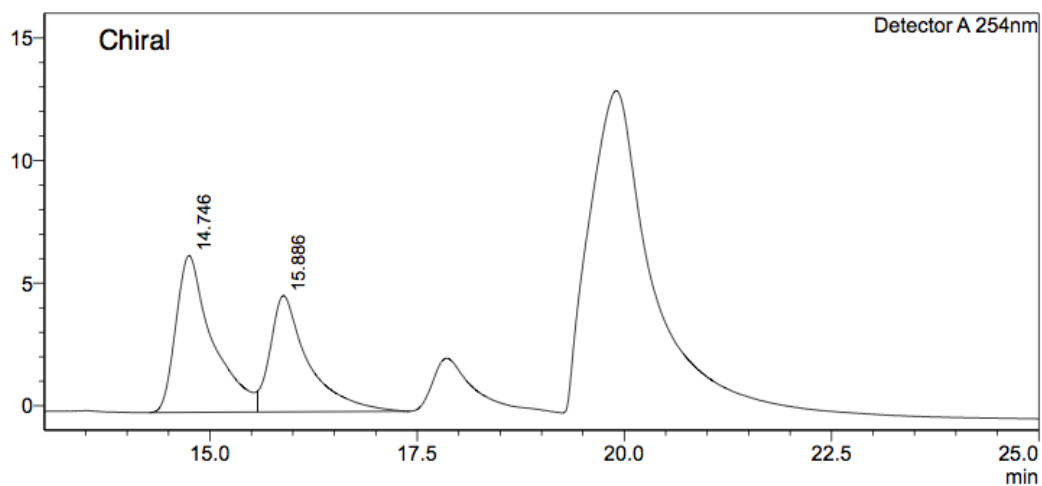
Major diastereomer ((2S,3S), 3I)



<Peak Table>

Detector A 254nm		
Peak#	Ret. Time	Area%
1	17.857	9.657
2	19.902	90.343
Total		100.000

Minor diastereomer ((2R,3S), 3I')

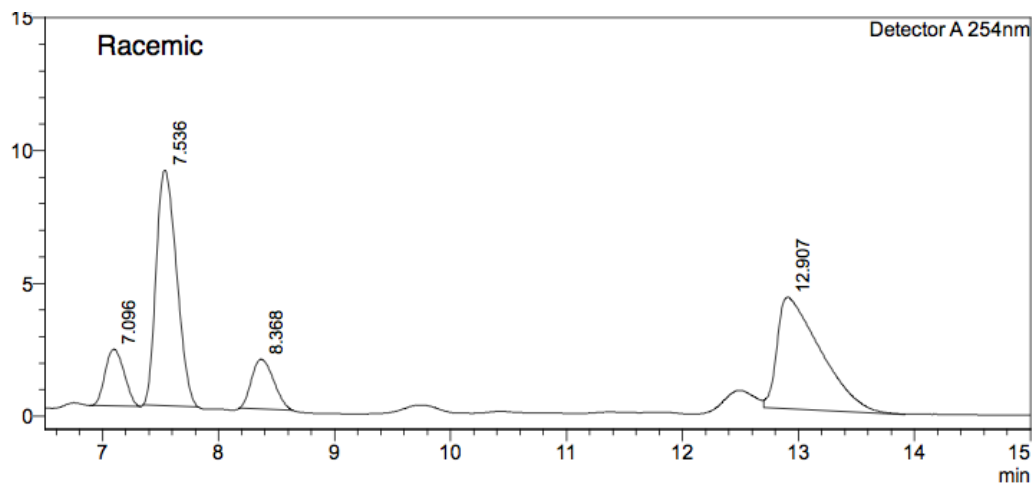


<Peak Table>

Detector A 254nm		
Peak#	Ret. Time	Area%
1	14.746	56.769
2	15.886	43.231
Total		100.000

(2S,3S)-Ethyl 2-fluoro-4-methyl-2-nitro-3-(nitromethyl)pentanoate (3m, major), (2R,3S)-Ethyl 2-fluoro-4-methyl-2-nitro-3-(nitromethyl)pentanoate (3m', minor); (diastereomeric mixture)

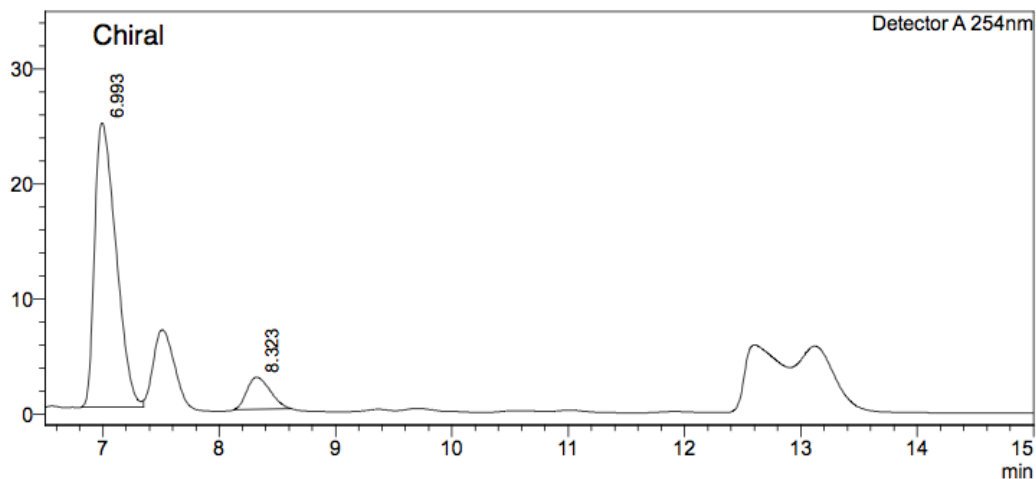
Diastereomers of the chiral and racemic products could not be fully separated. Resolution on HPLC of enantiomers of both diastereomers was achieved.



<Peak Table>

Detector A 254nm		
Peak#	Ret. Time	Area%
1	7.096	9.129
2	7.536	40.729
3	8.368	9.211
4	12.907	40.932
Total		100.000

Major diastereomer ((2S,3S), 3m)



<Peak Table>

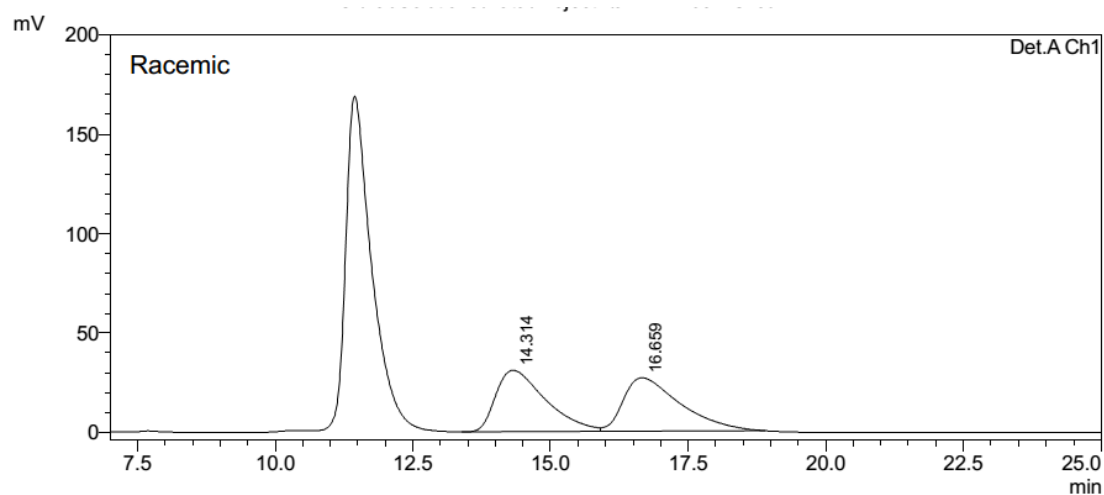
Detector A 254nm		
Peak#	Ret. Time	Area%
1	6.993	89.040
2	8.323	10.960
Total		100.000

B. HPLC chromatogram of the Mannich addition

Ethyl 3-((tert-butoxycarbonyl)amino)-2-fluoro-2-nitro-3-phenylpropanoate (13)

Diastereomers of the chiral and racemic products could not be fully separated. Resolution on HPLC of enantiomers of both diastereomers was achieved.

Diastereomer 1 (13)

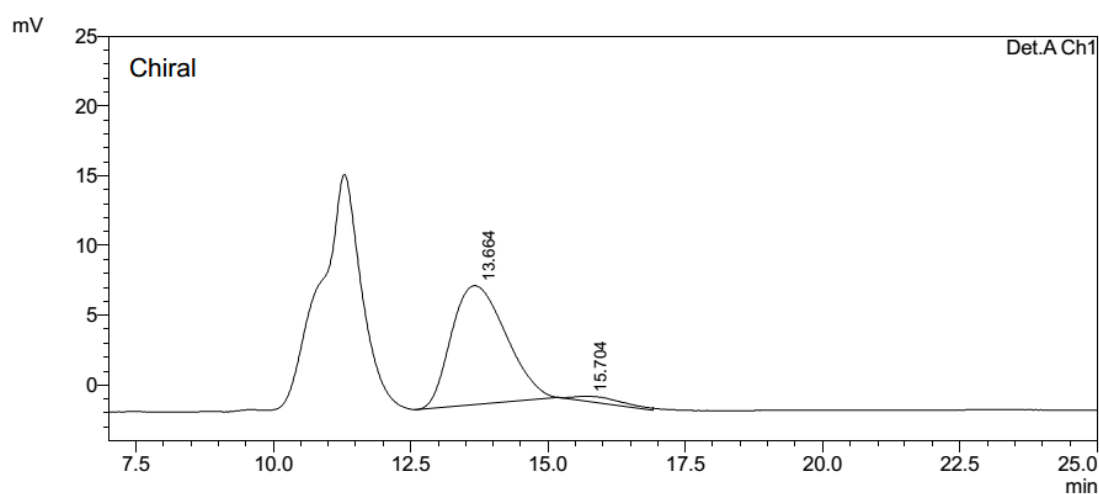


1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area %
1	14.314	50.008
2	16.659	49.992
Total		100.000



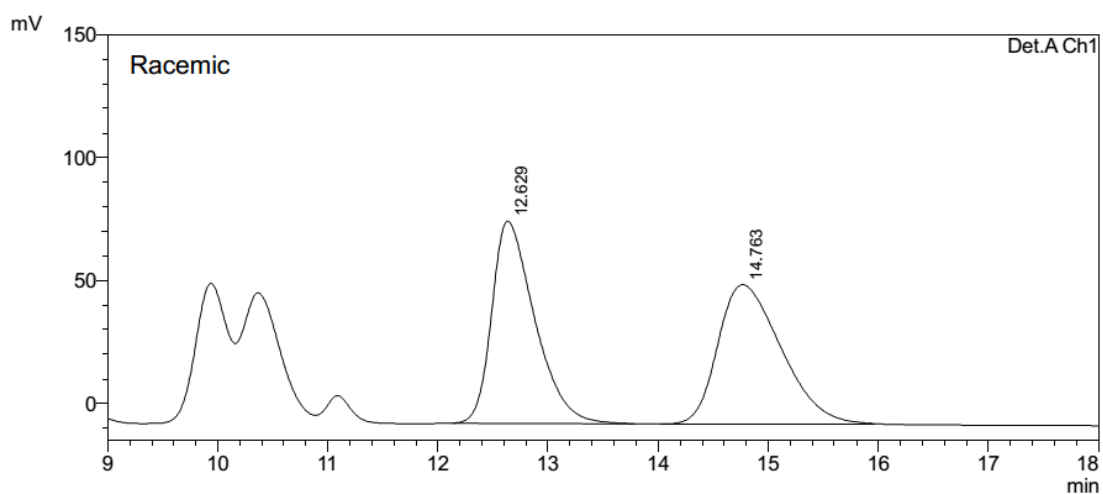
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area %
1	13.664	95.802
2	15.704	4.198
Total		100.000

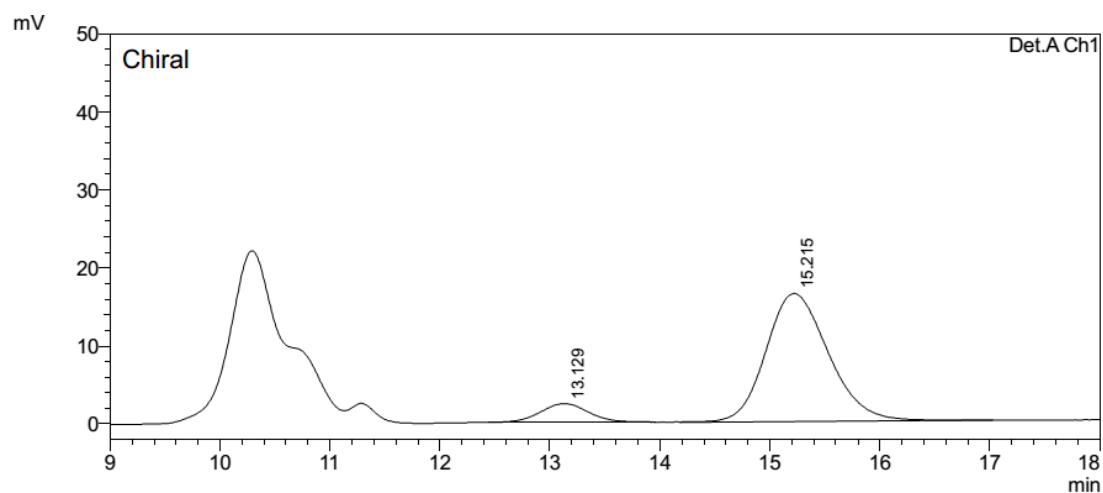
Diastereomer 2 (13'), racemate



PeakTable
Detector A Ch1 254nm

Peak#	Ret. Time	Area %
1	12.629	49.706
2	14.763	50.294
Total		100.000

Diastereomer 2 (13'), chiral



PeakTable
Detector A Ch1 254nm

Peak#	Ret. Time	Area %
1	13.129	10.141
2	15.215	89.859
Total		100.000

C. X-Ray Crystallographic Analysis and Determination of Configurations of Products

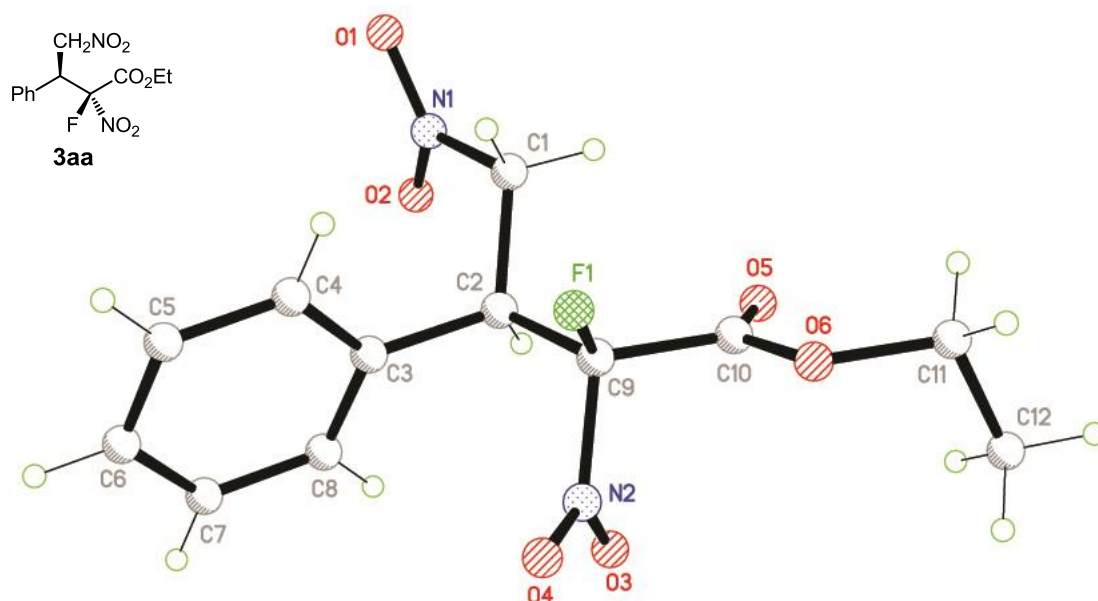


Table 1. Crystal data and structure refinement for D610.

Identification code	D610	
Empirical formula	C ₁₂ H ₁₃ F N ₂ O ₆	
Formula weight	300.24	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 5.5351(6) Å	α = 90°.
	b = 11.2034(12) Å	β = 90°.
	c = 21.678(2) Å	γ = 90°.
Volume	1344.3(3) Å ³	
Z	4	
Density (calculated)	1.483 Mg/m ³	
Absorption coefficient	1.117 mm ⁻¹	
F(000)	624	
Crystal size	0.280 x 0.150 x 0.130 mm ³	
Theta range for data collection	4.078 to 72.323°.	
Index ranges	-6 ≤ h ≤ 6, -13 ≤ k ≤ 13, -26 ≤ l ≤ 26	
Reflections collected	22572	
Independent reflections	2637 [R(int) = 0.0240]	
Completeness to theta = 67.679°	99.9 %	

Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.753 and 0.6796
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	2637 / 0 / 191
Goodness-of-fit on F ²	1.094
Final R indices [I>2sigma(I)]	R1 = 0.0250, wR2 = 0.0655
R indices (all data)	R1 = 0.0253, wR2 = 0.0658
Absolute structure parameter	0.05(2)
Extinction coefficient	n/a
Largest diff. peak and hole	0.167 and -0.248 e.Å ⁻³

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for D610. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
F(1)	10814(2)	2448(1)	2094(1)	26(1)
O(1)	6458(3)	-571(1)	842(1)	39(1)
O(2)	3585(2)	486(1)	1233(1)	25(1)
O(3)	5862(3)	3868(1)	2673(1)	39(1)
O(4)	9229(3)	4521(1)	2280(1)	46(1)
O(5)	6784(2)	1154(1)	3076(1)	24(1)
O(6)	10238(2)	2174(1)	3268(1)	21(1)
N(1)	5692(3)	170(1)	1206(1)	20(1)
N(2)	7823(3)	3743(1)	2429(1)	27(1)
C(1)	7460(3)	689(1)	1658(1)	18(1)
C(2)	6773(3)	1978(1)	1805(1)	15(1)
C(3)	6797(3)	2784(1)	1239(1)	15(1)
C(4)	8665(3)	2734(1)	807(1)	18(1)
C(5)	8650(3)	3487(1)	297(1)	20(1)
C(6)	6786(3)	4299(1)	216(1)	20(1)
C(7)	4930(3)	4356(2)	644(1)	20(1)
C(8)	4932(3)	3604(1)	1156(1)	18(1)
C(9)	8504(3)	2445(1)	2299(1)	17(1)
C(10)	8370(3)	1821(1)	2935(1)	17(1)
C(11)	10490(3)	1630(2)	3880(1)	26(1)
C(12)	8971(4)	2275(2)	4347(1)	32(1)

Table 3. Bond lengths [Å] and angles [°] for D610.

F(1)-C(9)	1.3534(18)
O(1)-N(1)	1.2208(19)
O(2)-N(1)	1.2204(19)
O(3)-N(2)	1.215(2)
O(4)-N(2)	1.212(2)
O(5)-C(10)	1.192(2)
O(6)-C(10)	1.3210(19)
O(6)-C(11)	1.4676(18)
N(1)-C(1)	1.5021(19)
N(2)-C(9)	1.528(2)
C(1)-C(2)	1.527(2)
C(2)-C(3)	1.523(2)
C(2)-C(9)	1.531(2)
C(3)-C(8)	1.394(2)
C(3)-C(4)	1.396(2)
C(4)-C(5)	1.391(2)
C(5)-C(6)	1.387(2)
C(6)-C(7)	1.387(2)
C(7)-C(8)	1.392(2)
C(9)-C(10)	1.547(2)
C(11)-C(12)	1.501(3)
C(10)-O(6)-C(11)	116.32(13)
O(2)-N(1)-O(1)	124.10(15)
O(2)-N(1)-C(1)	118.60(13)
O(1)-N(1)-C(1)	117.27(14)
O(4)-N(2)-O(3)	127.36(17)
O(4)-N(2)-C(9)	118.45(16)
O(3)-N(2)-C(9)	114.18(14)
N(1)-C(1)-C(2)	109.87(12)
C(3)-C(2)-C(1)	113.06(12)
C(3)-C(2)-C(9)	110.85(12)
C(1)-C(2)-C(9)	108.26(12)
C(8)-C(3)-C(4)	119.23(14)
C(8)-C(3)-C(2)	119.29(13)
C(4)-C(3)-C(2)	121.47(13)

C(5)-C(4)-C(3)	120.26(14)
C(6)-C(5)-C(4)	120.28(14)
C(7)-C(6)-C(5)	119.70(14)
C(6)-C(7)-C(8)	120.33(15)
C(7)-C(8)-C(3)	120.20(14)
F(1)-C(9)-N(2)	106.92(12)
F(1)-C(9)-C(2)	111.22(12)
N(2)-C(9)-C(2)	107.42(12)
F(1)-C(9)-C(10)	109.84(12)
N(2)-C(9)-C(10)	104.75(12)
C(2)-C(9)-C(10)	116.08(12)
O(5)-C(10)-O(6)	128.67(14)
O(5)-C(10)-C(9)	123.10(14)
O(6)-C(10)-C(9)	108.23(12)
O(6)-C(11)-C(12)	110.88(14)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for D610. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
F(1)	14(1)	45(1)	19(1)	4(1)	1(1)	-7(1)
O(1)	48(1)	36(1)	34(1)	-20(1)	-8(1)	9(1)
O(2)	21(1)	29(1)	24(1)	1(1)	-6(1)	-3(1)
O(3)	54(1)	34(1)	29(1)	-9(1)	-2(1)	20(1)
O(4)	71(1)	24(1)	43(1)	12(1)	-28(1)	-23(1)
O(5)	26(1)	26(1)	19(1)	3(1)	0(1)	-8(1)
O(6)	22(1)	26(1)	16(1)	4(1)	-4(1)	-3(1)
N(1)	26(1)	16(1)	17(1)	1(1)	-2(1)	-2(1)
N(2)	43(1)	18(1)	19(1)	0(1)	-12(1)	-2(1)
C(1)	18(1)	18(1)	18(1)	0(1)	-2(1)	0(1)
C(2)	14(1)	17(1)	14(1)	0(1)	1(1)	0(1)
C(3)	16(1)	15(1)	14(1)	-2(1)	-1(1)	-3(1)
C(4)	16(1)	20(1)	17(1)	-2(1)	0(1)	1(1)
C(5)	21(1)	24(1)	14(1)	-2(1)	3(1)	-2(1)
C(6)	26(1)	18(1)	15(1)	1(1)	-1(1)	-3(1)

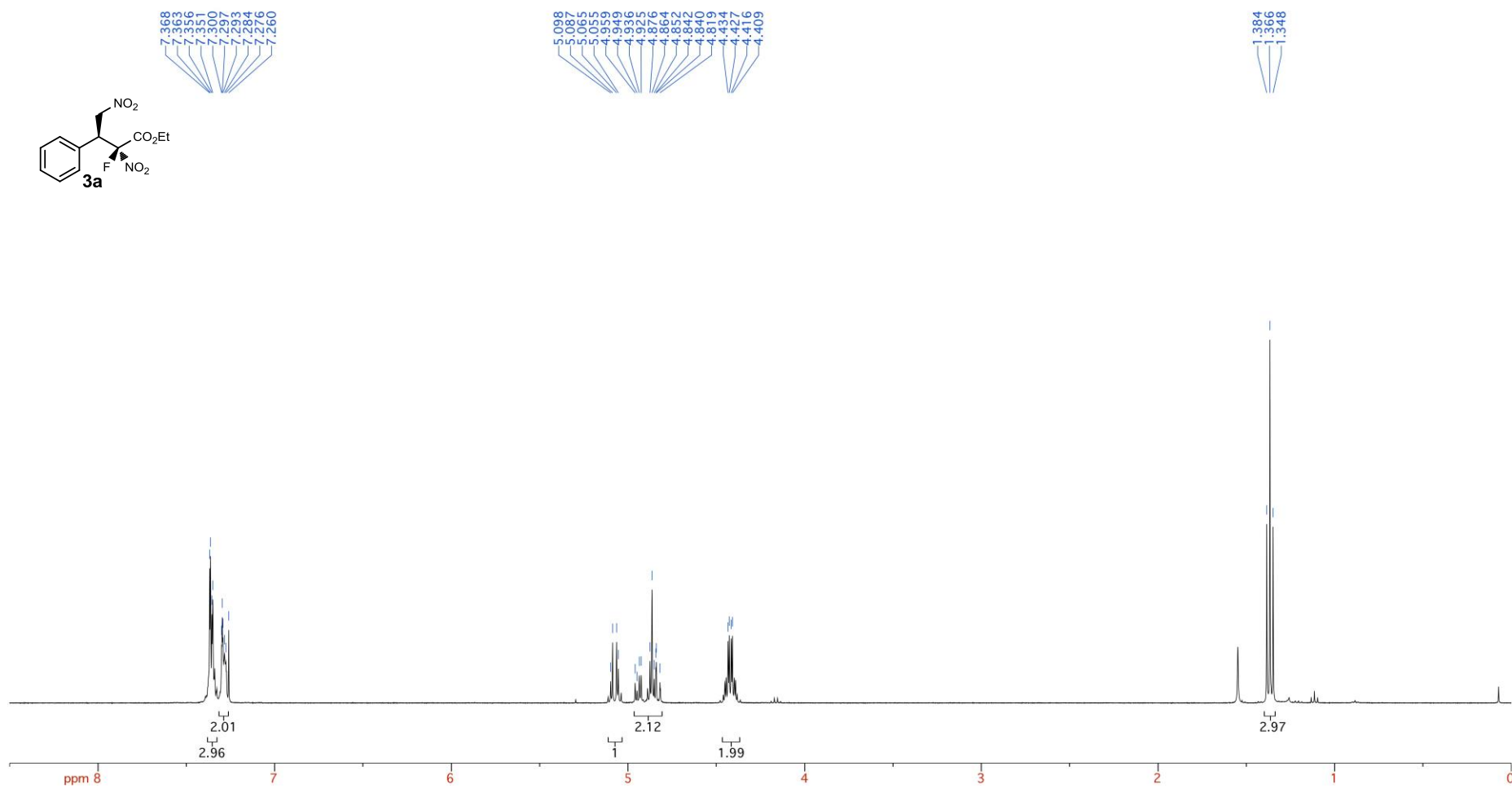
C(7)	22(1)	17(1)	21(1)	1(1)	-2(1)	3(1)
C(8)	16(1)	19(1)	18(1)	-1(1)	3(1)	0(1)
C(9)	15(1)	18(1)	17(1)	1(1)	0(1)	-2(1)
C(10)	19(1)	17(1)	15(1)	1(1)	0(1)	2(1)
C(11)	29(1)	31(1)	17(1)	7(1)	-7(1)	-2(1)
C(12)	49(1)	30(1)	18(1)	-2(1)	-1(1)	-9(1)

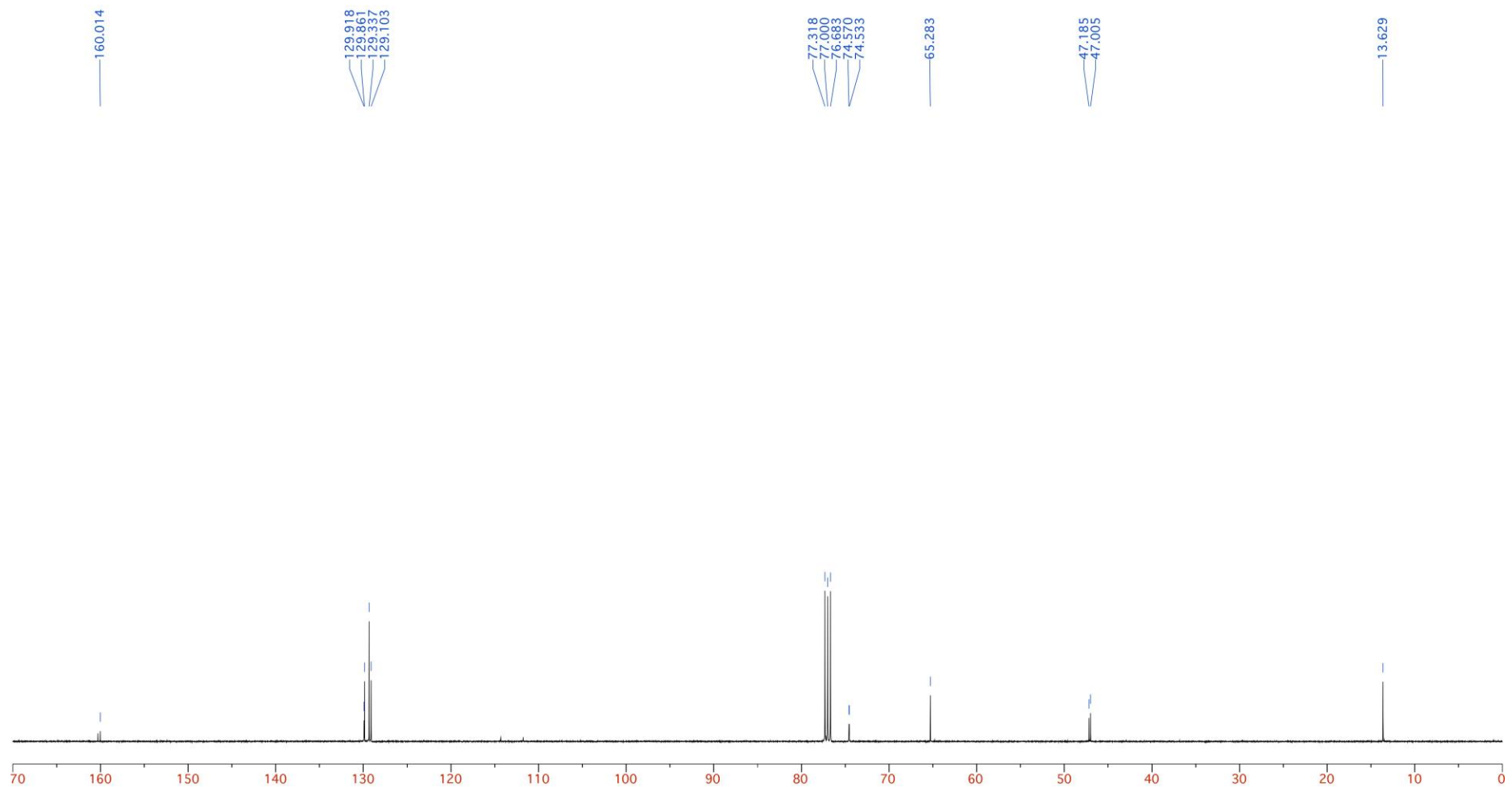
Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for D610.

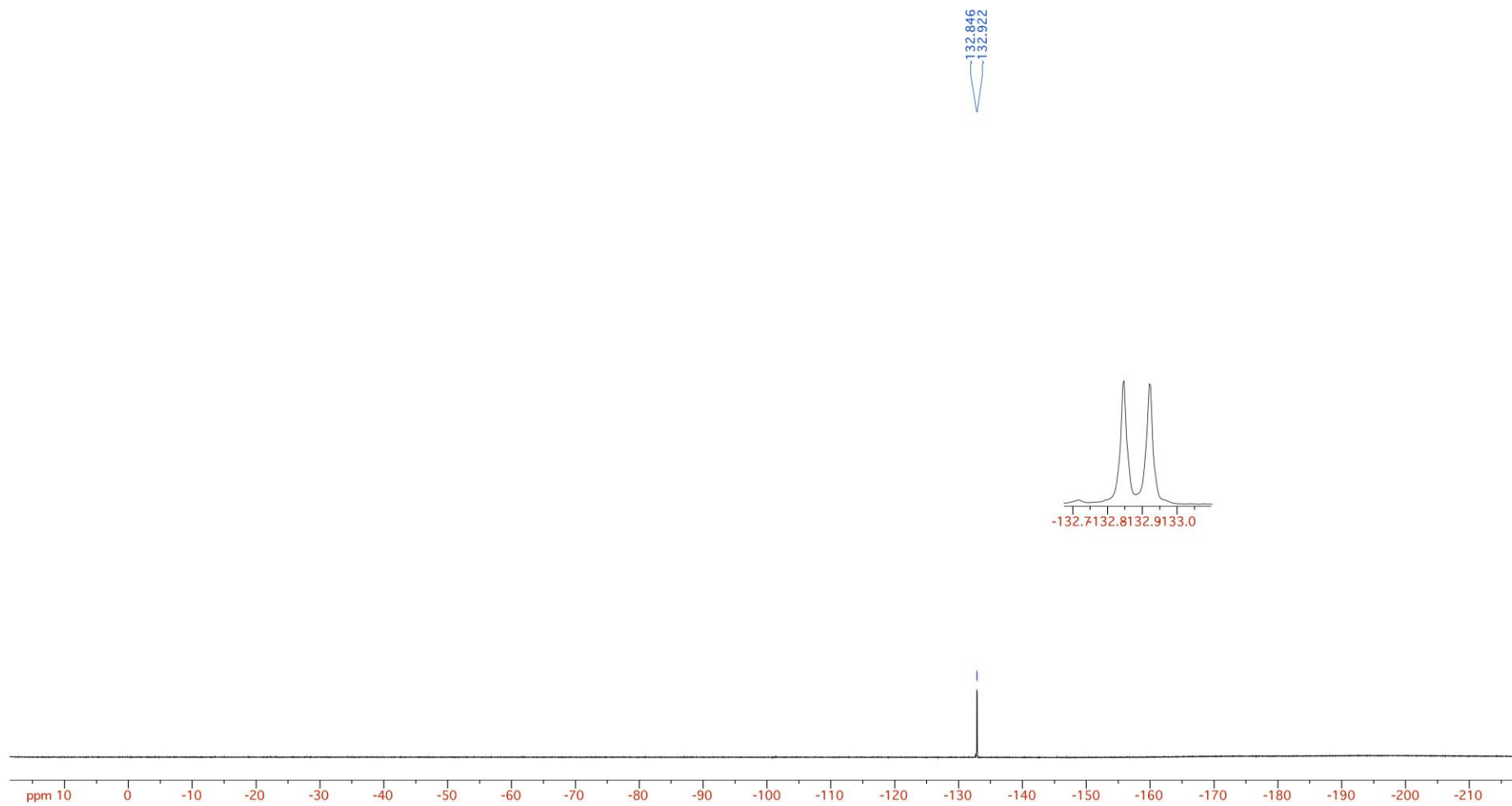
	x	y	z	U(eq)
H(1A)	9108	663	1482	21
H(1B)	7454	210	2042	21
H(2)	5102	1981	1980	18
H(4)	9952	2183	862	21
H(5)	9922	3446	4	24
H(6)	6781	4814	-133	24
H(7)	3651	4911	589	24
H(8)	3659	3650	1448	21
H(11A)	12205	1656	4009	31
H(11B)	9988	783	3861	31
H(12A)	9491	3110	4372	49
H(12B)	9159	1895	4751	49
H(12C)	7271	2243	4221	49

D. NMR Spectra of the Michael Products

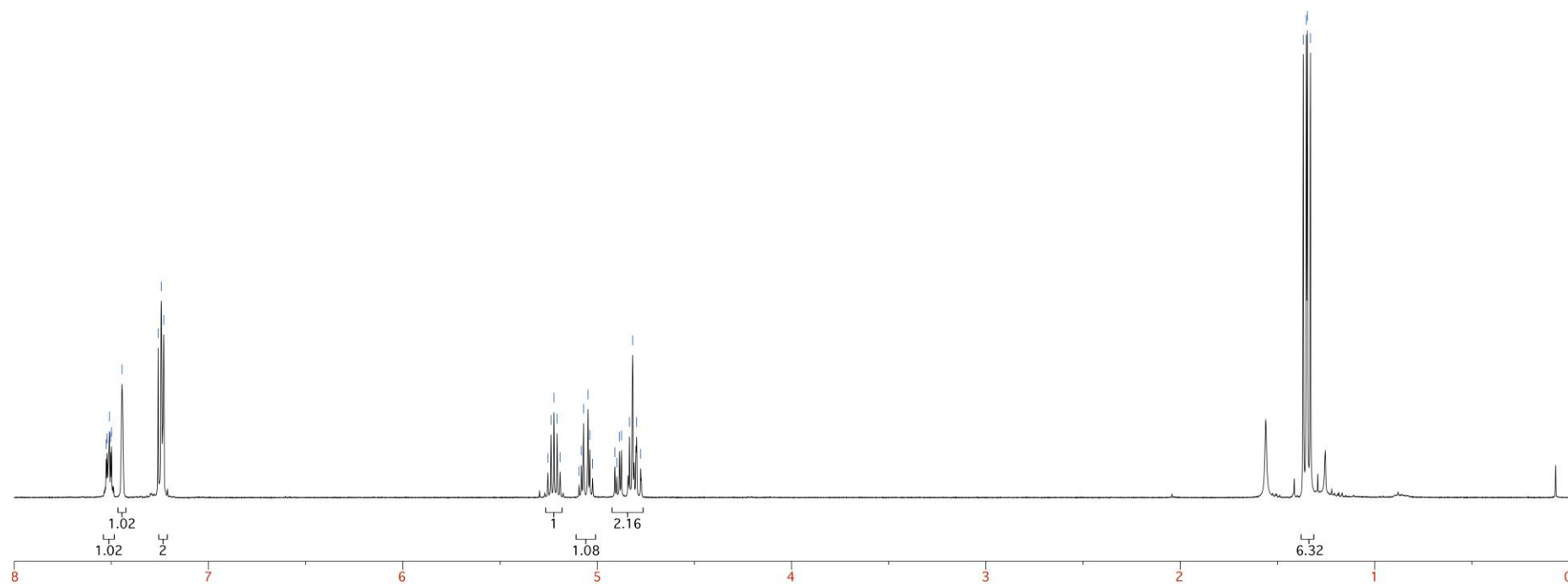
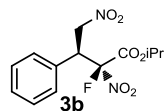
Major diastereomer (3a)

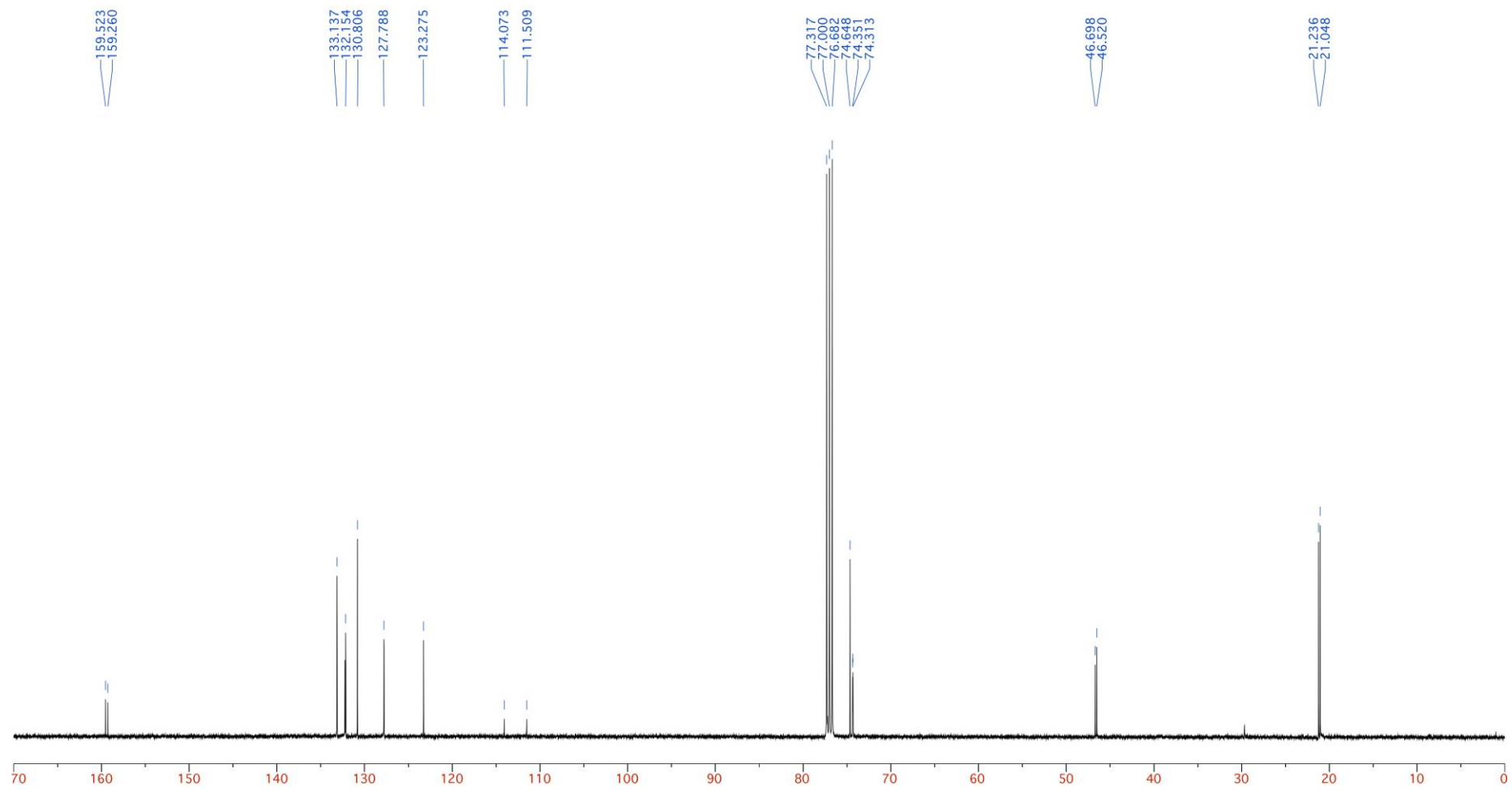


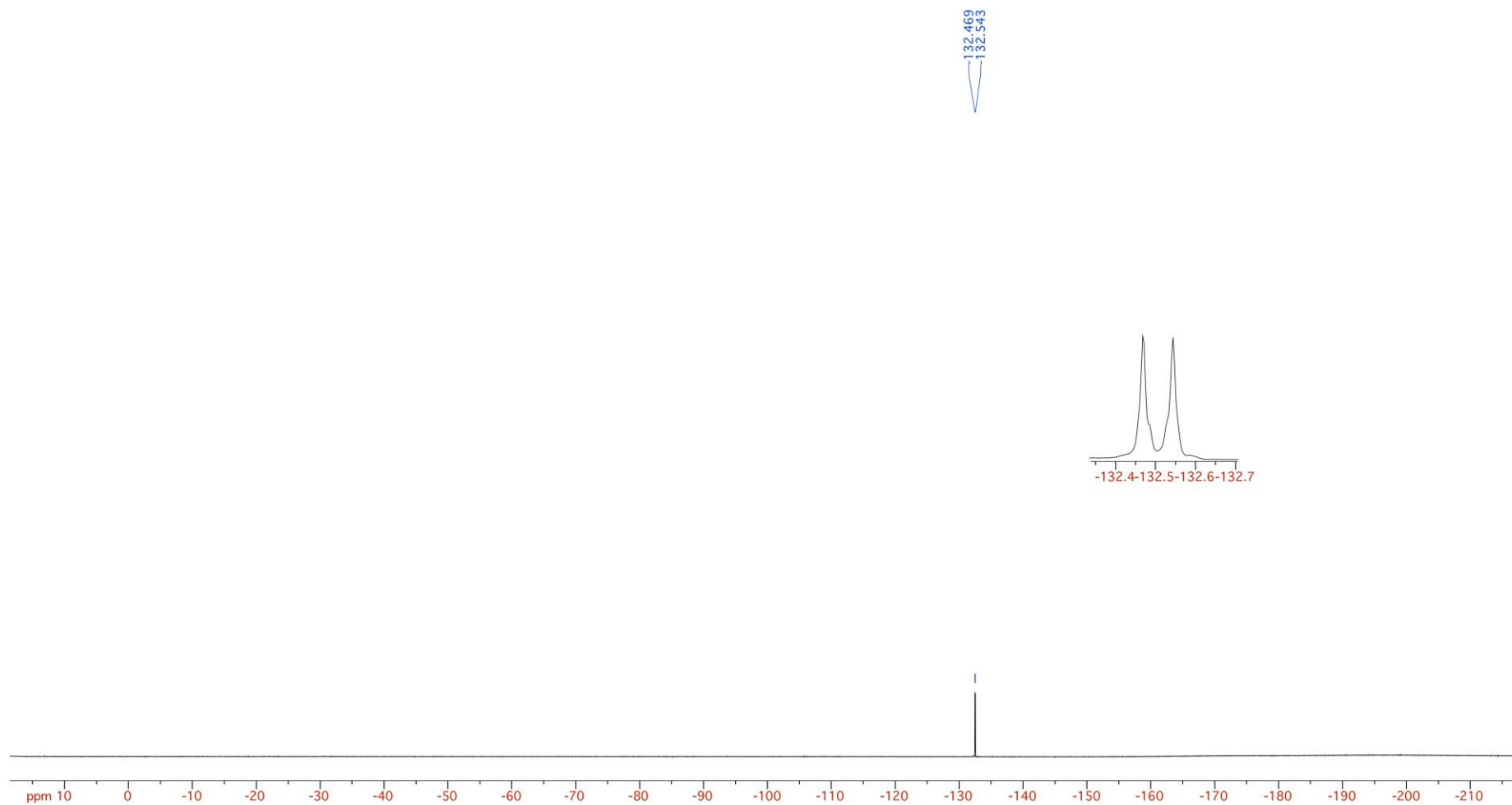




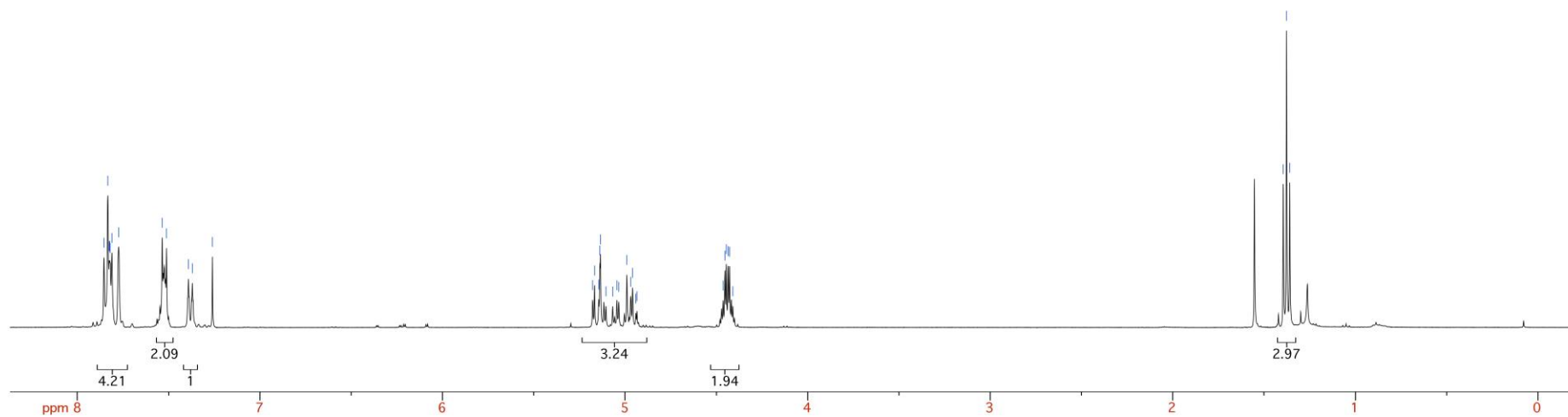
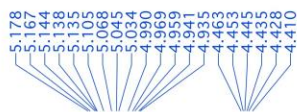
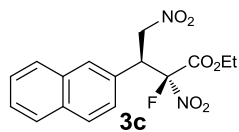
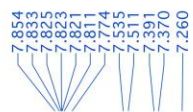
Major diastereomer (3b)

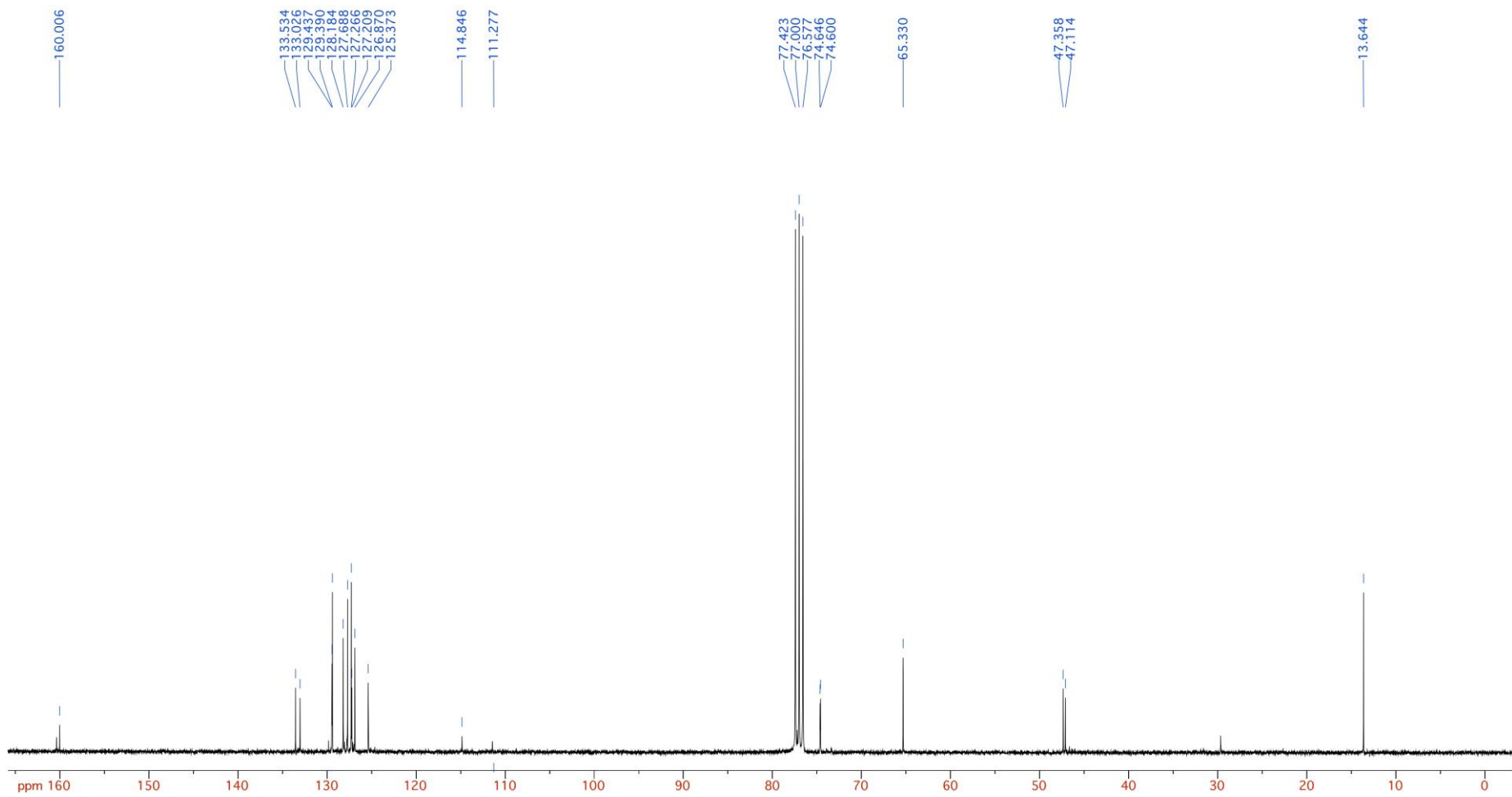


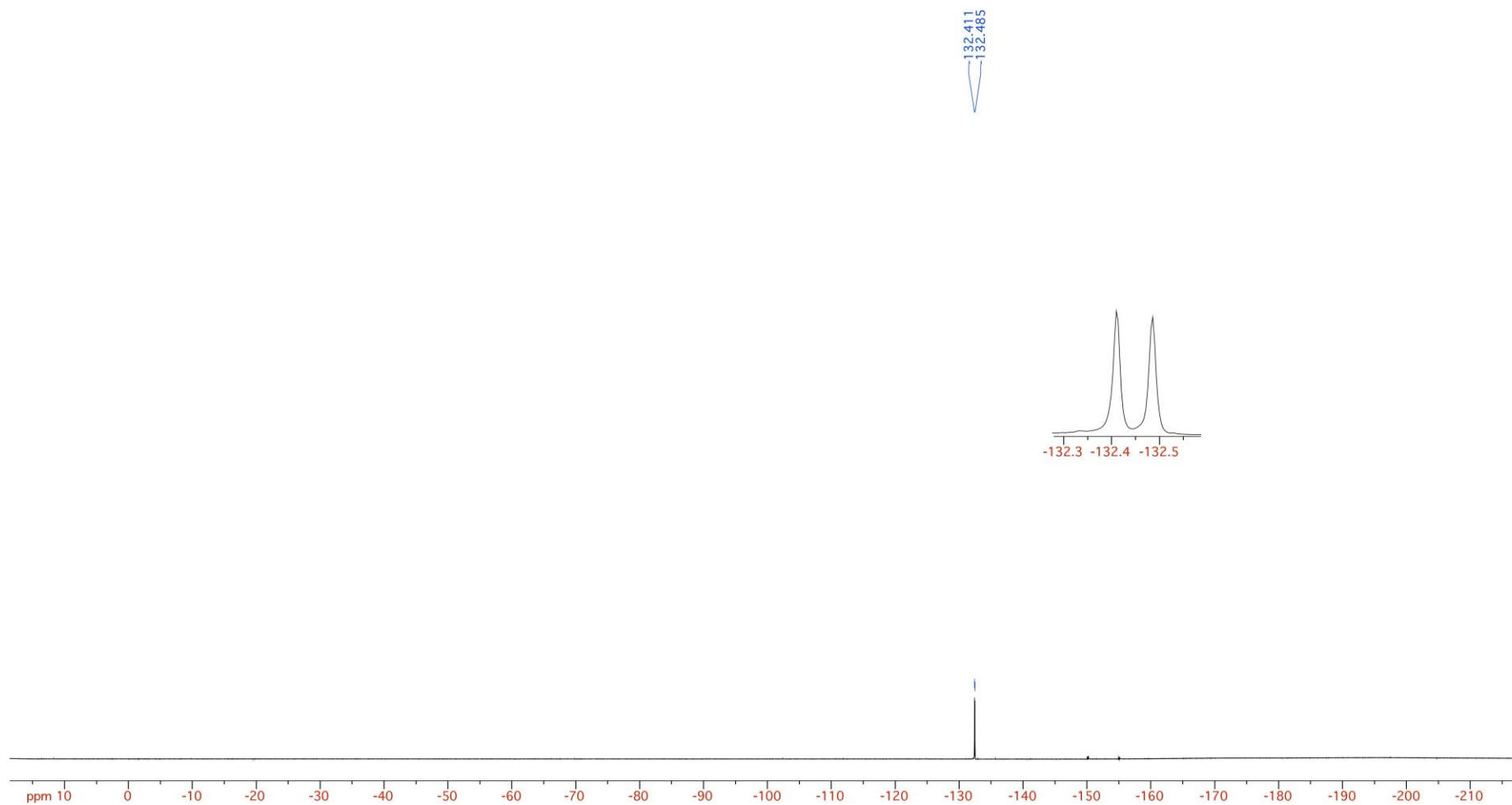




Major diastereomer (3c)

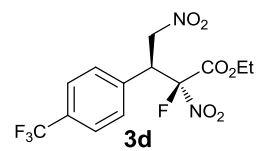






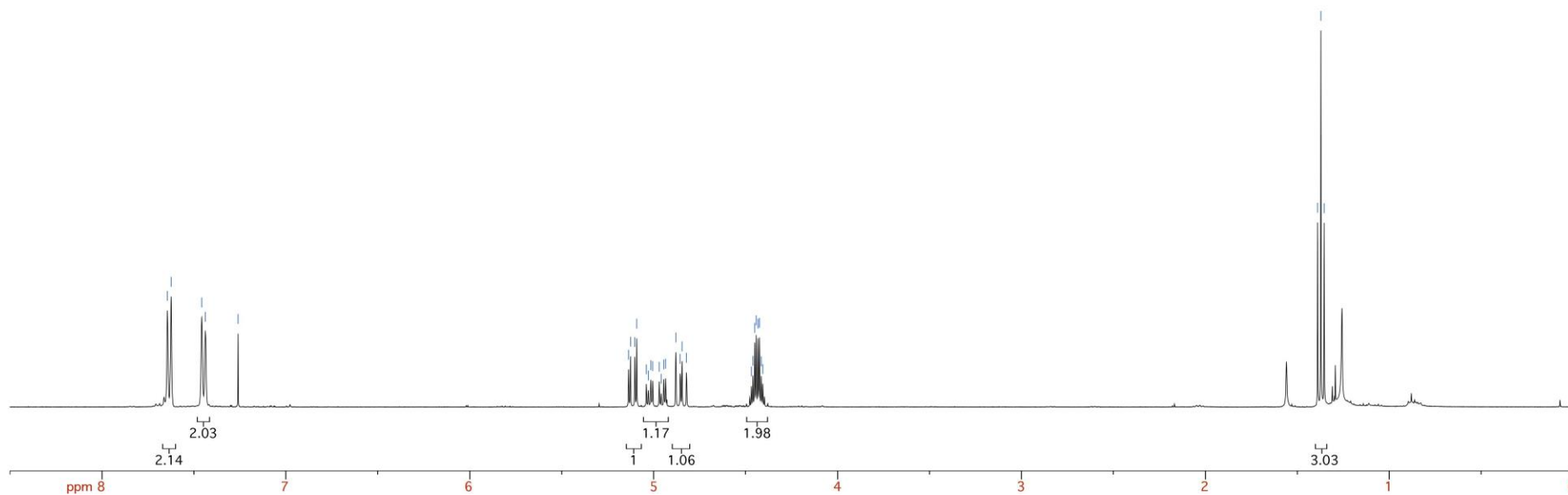
Major diastereomer (3d)

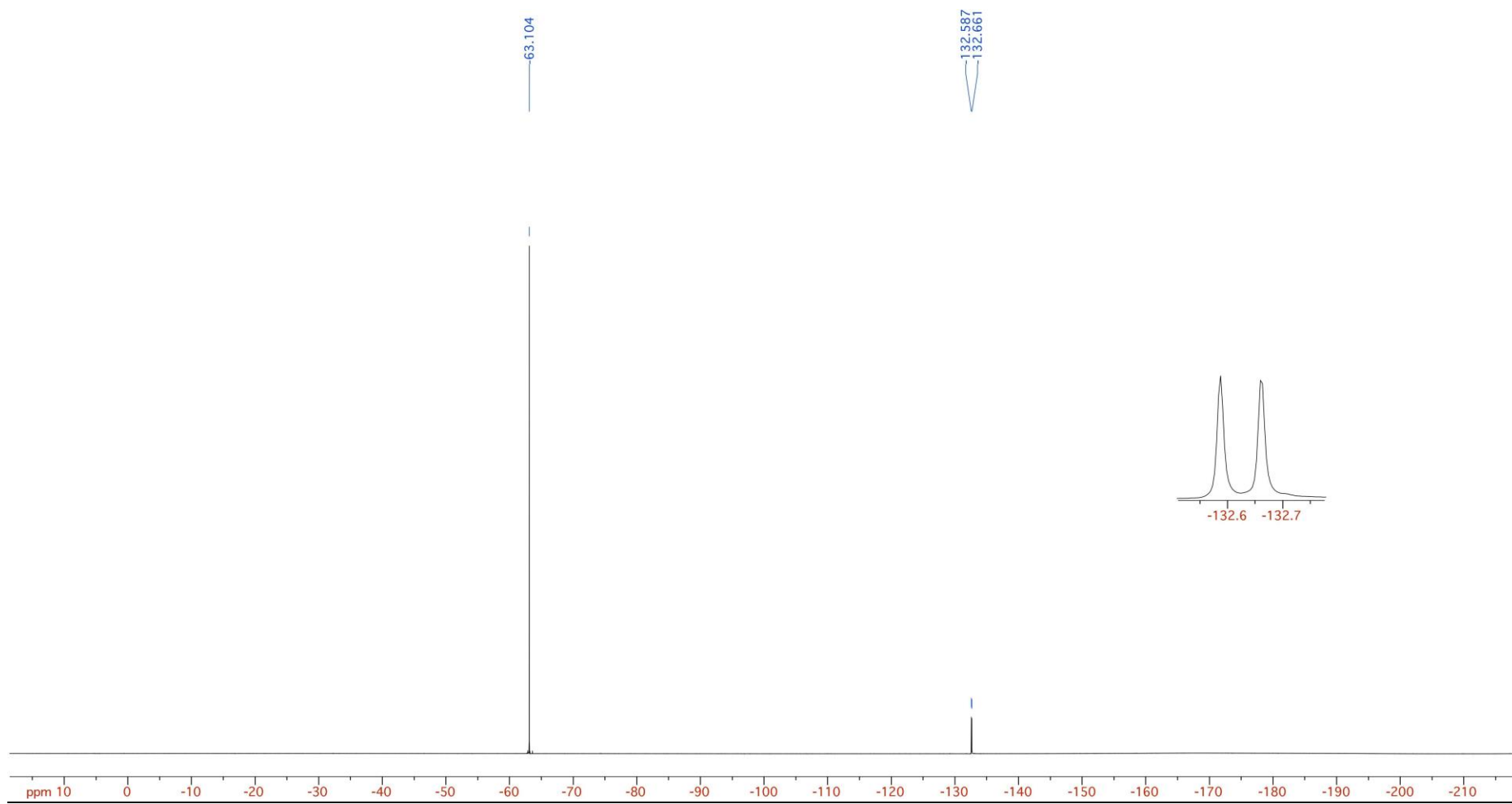
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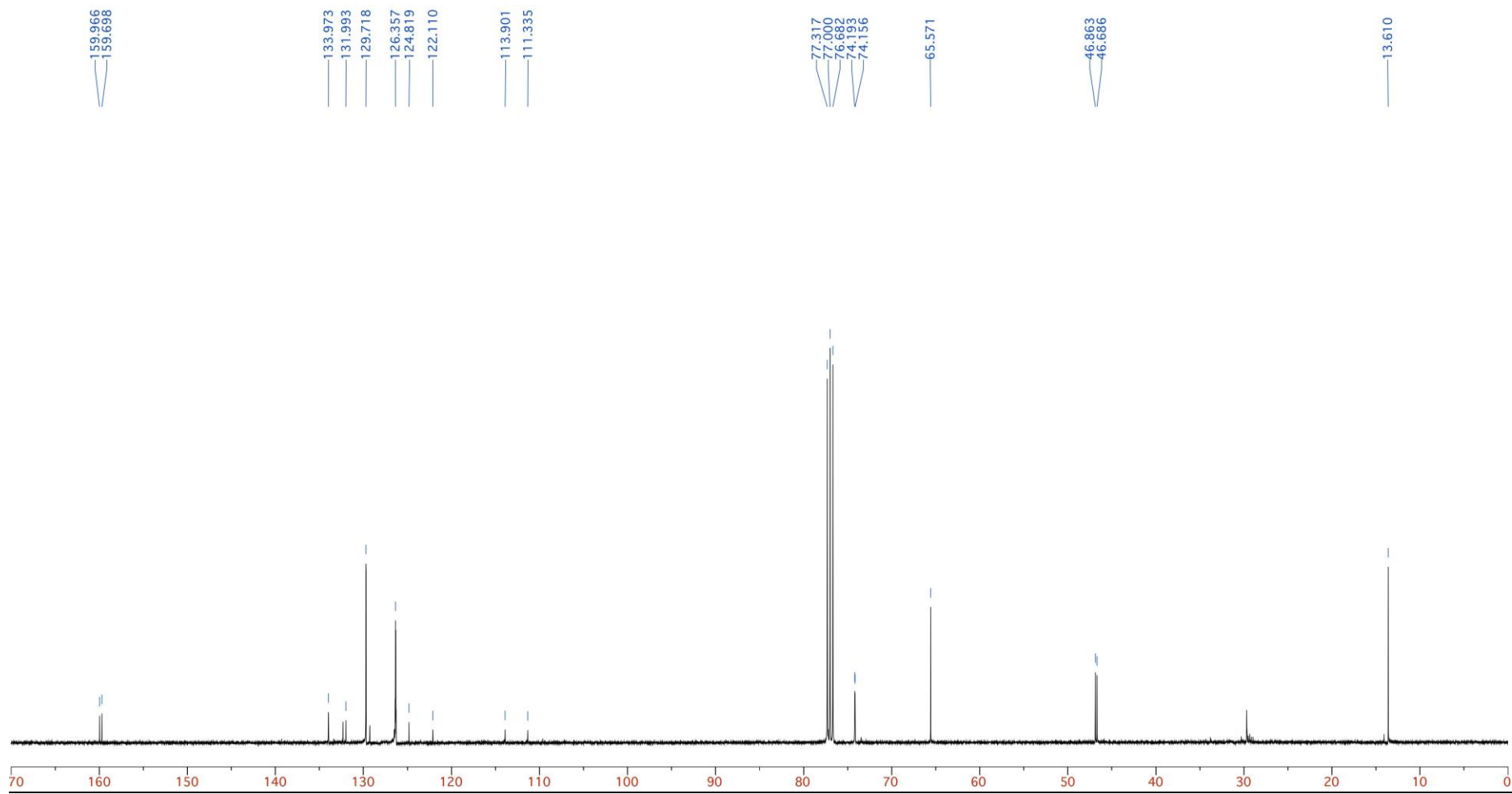


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4.910
4.890
4.870
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4.830
4.810
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0.010

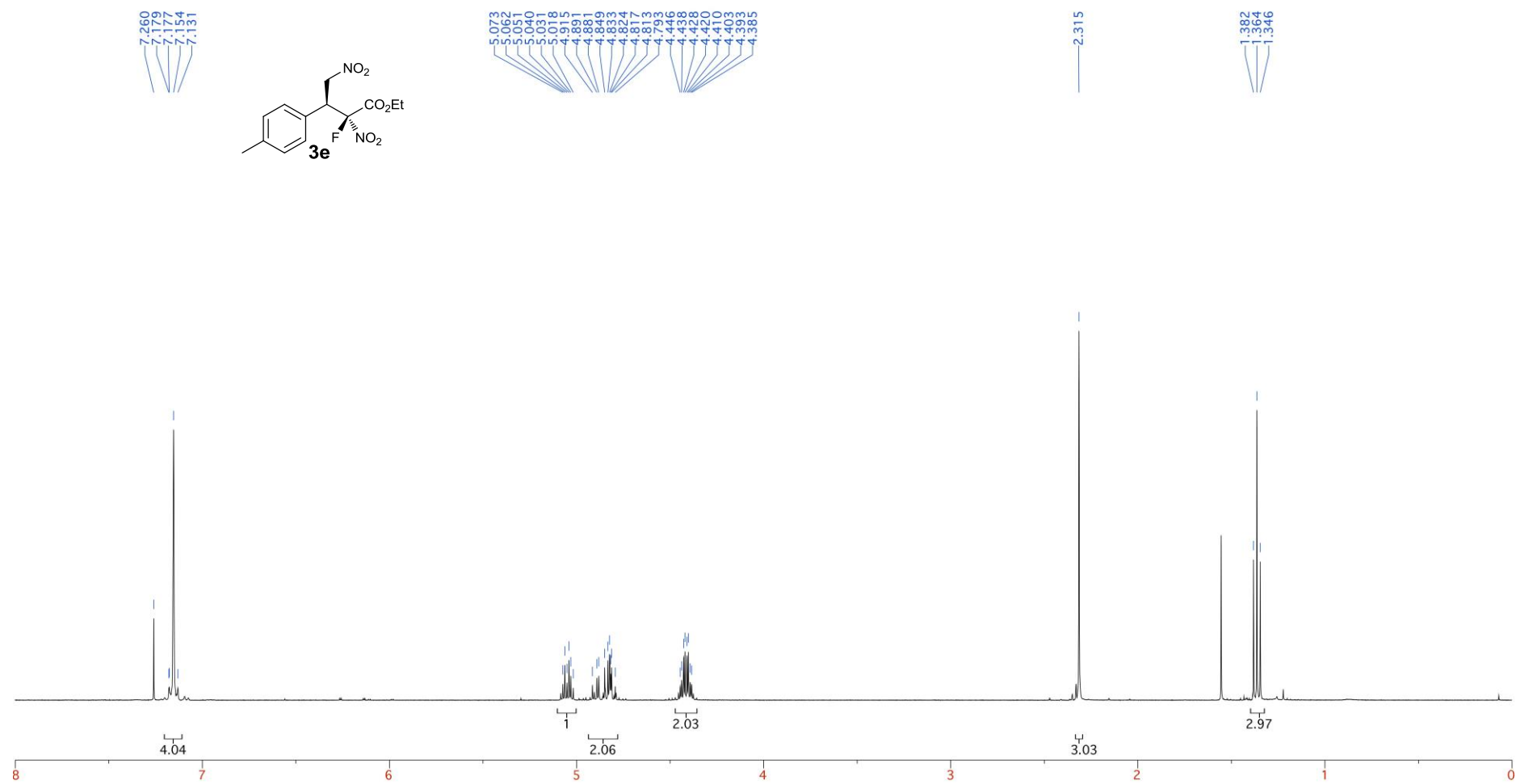
1.390
1.372
1.354

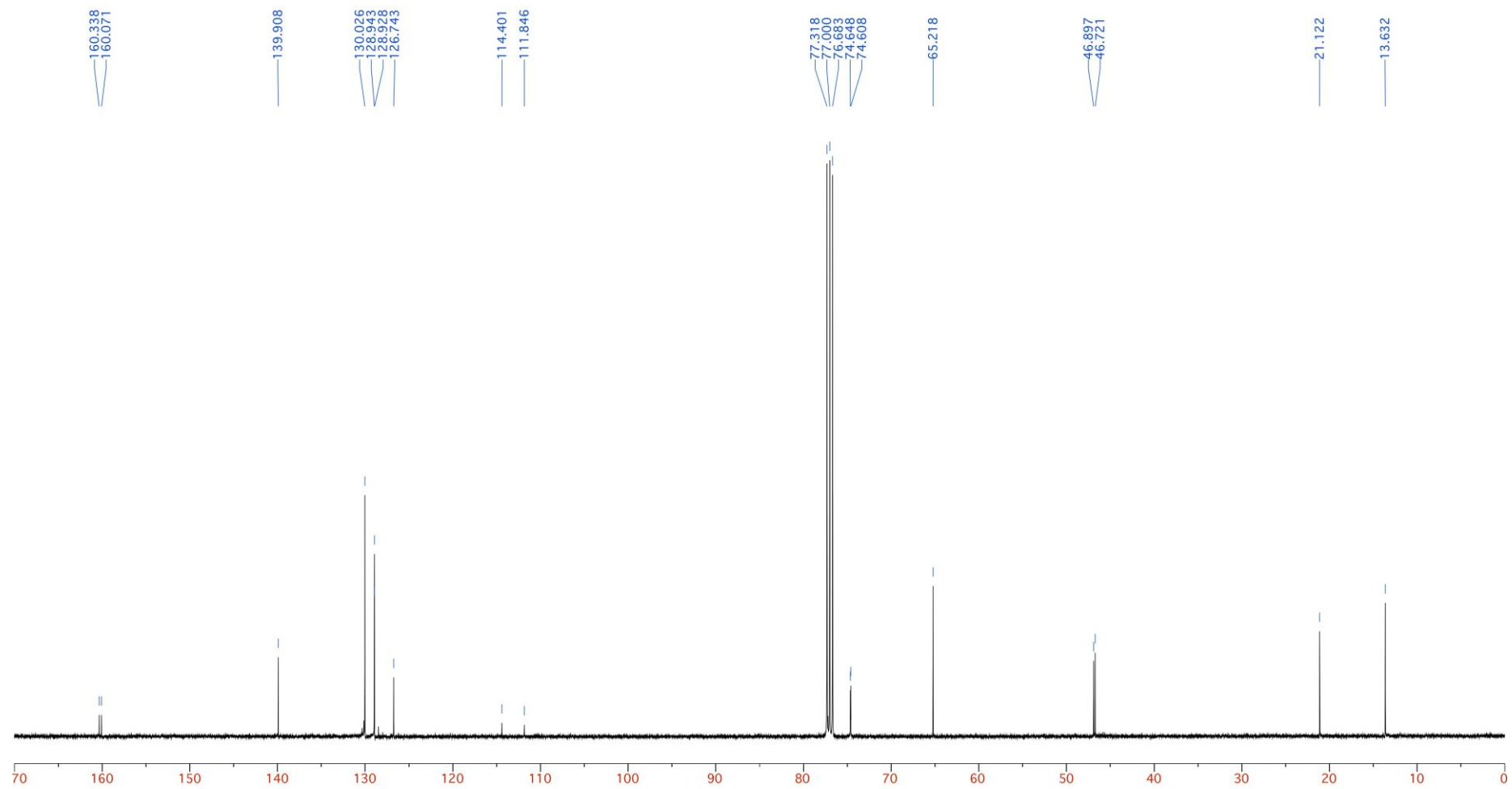


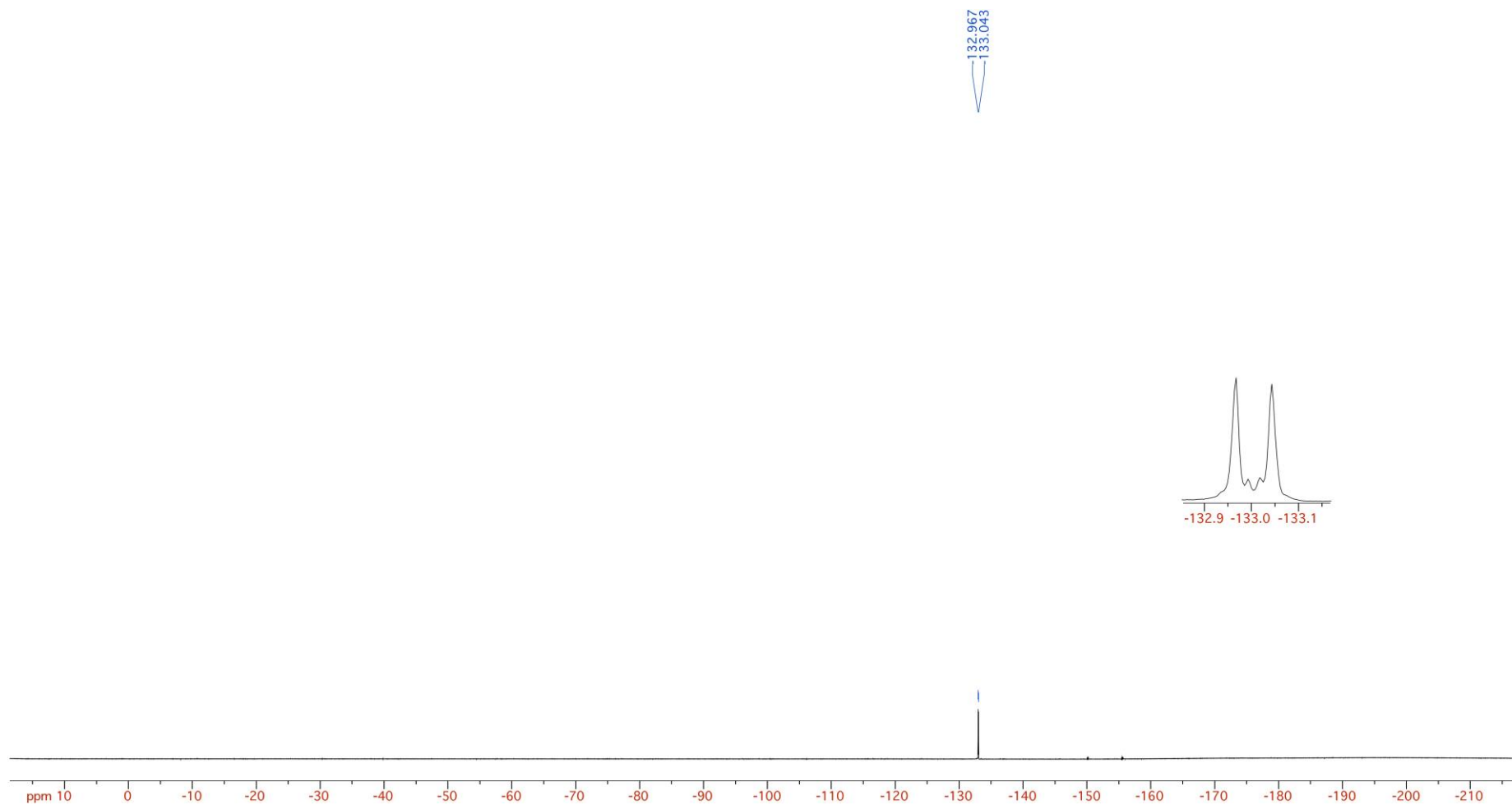




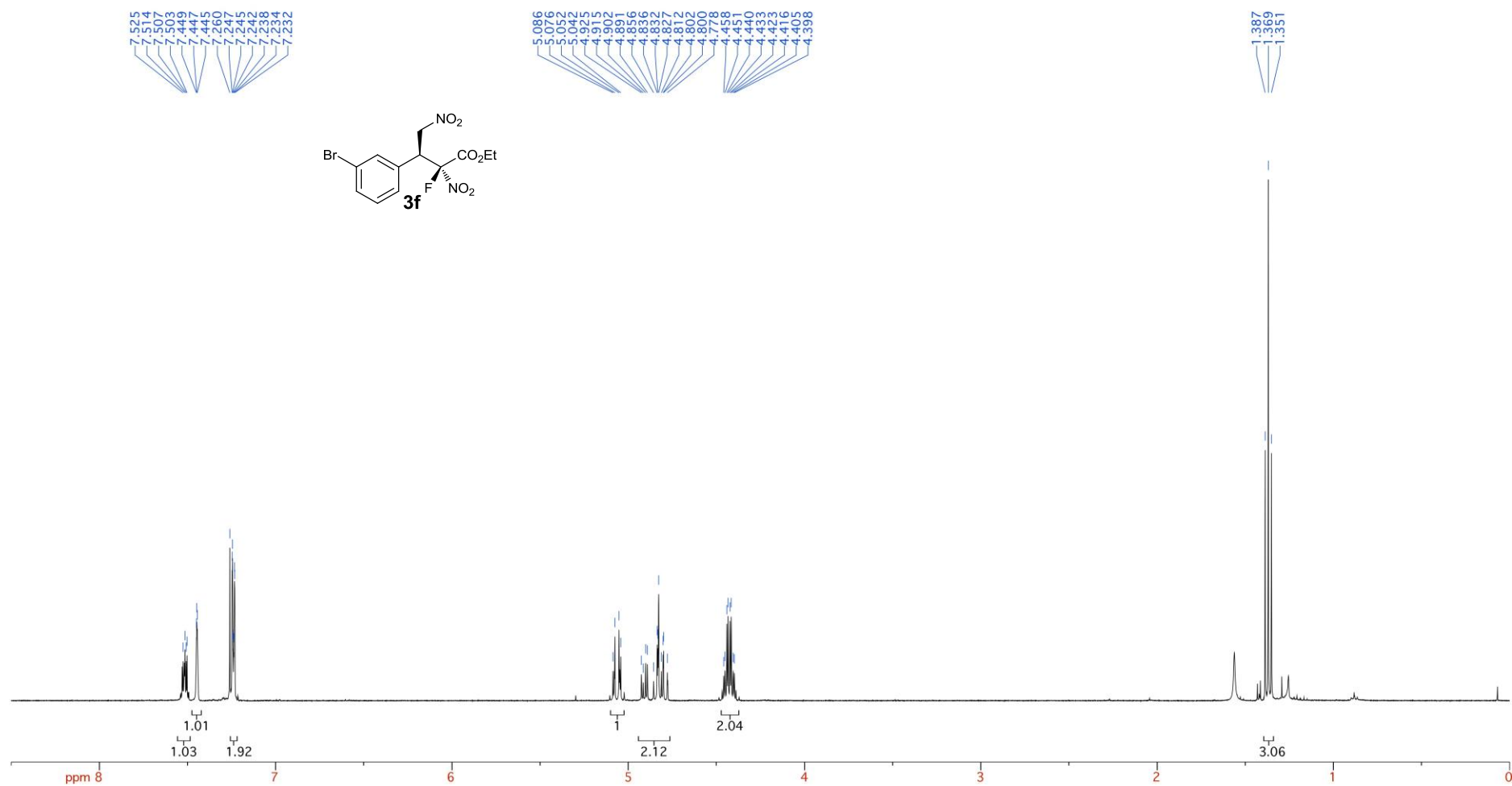
Major diastereomer (3e)

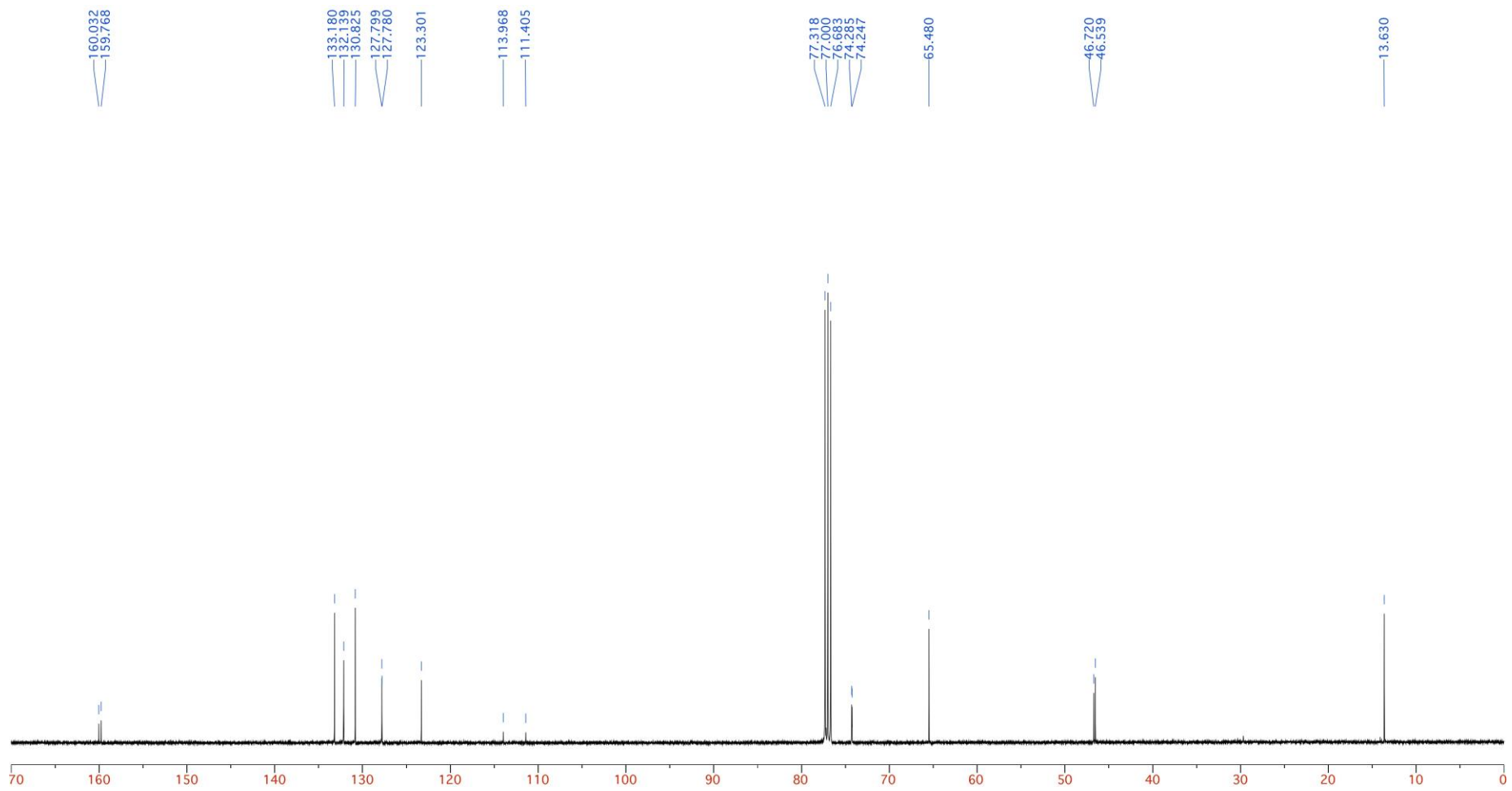


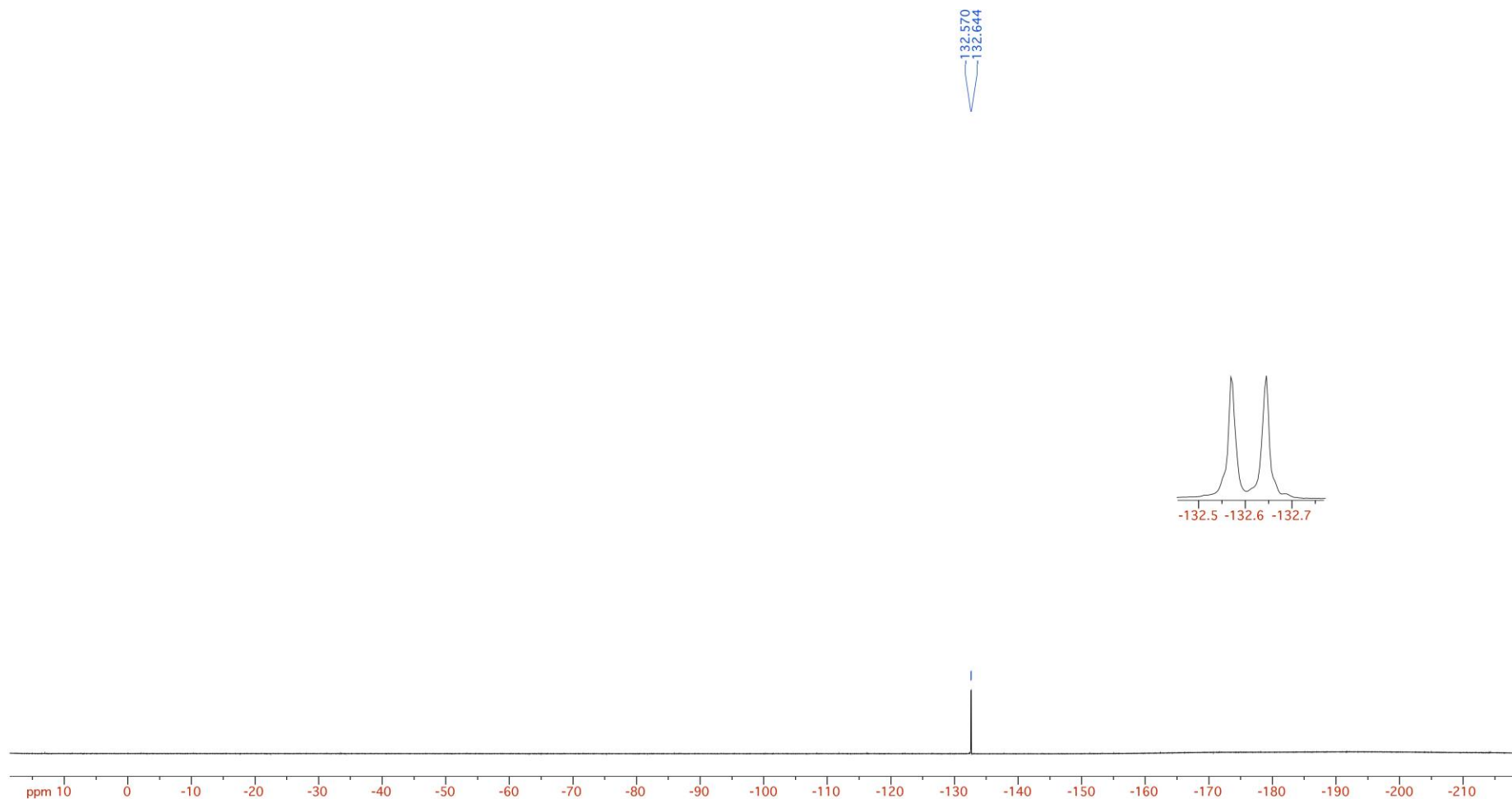




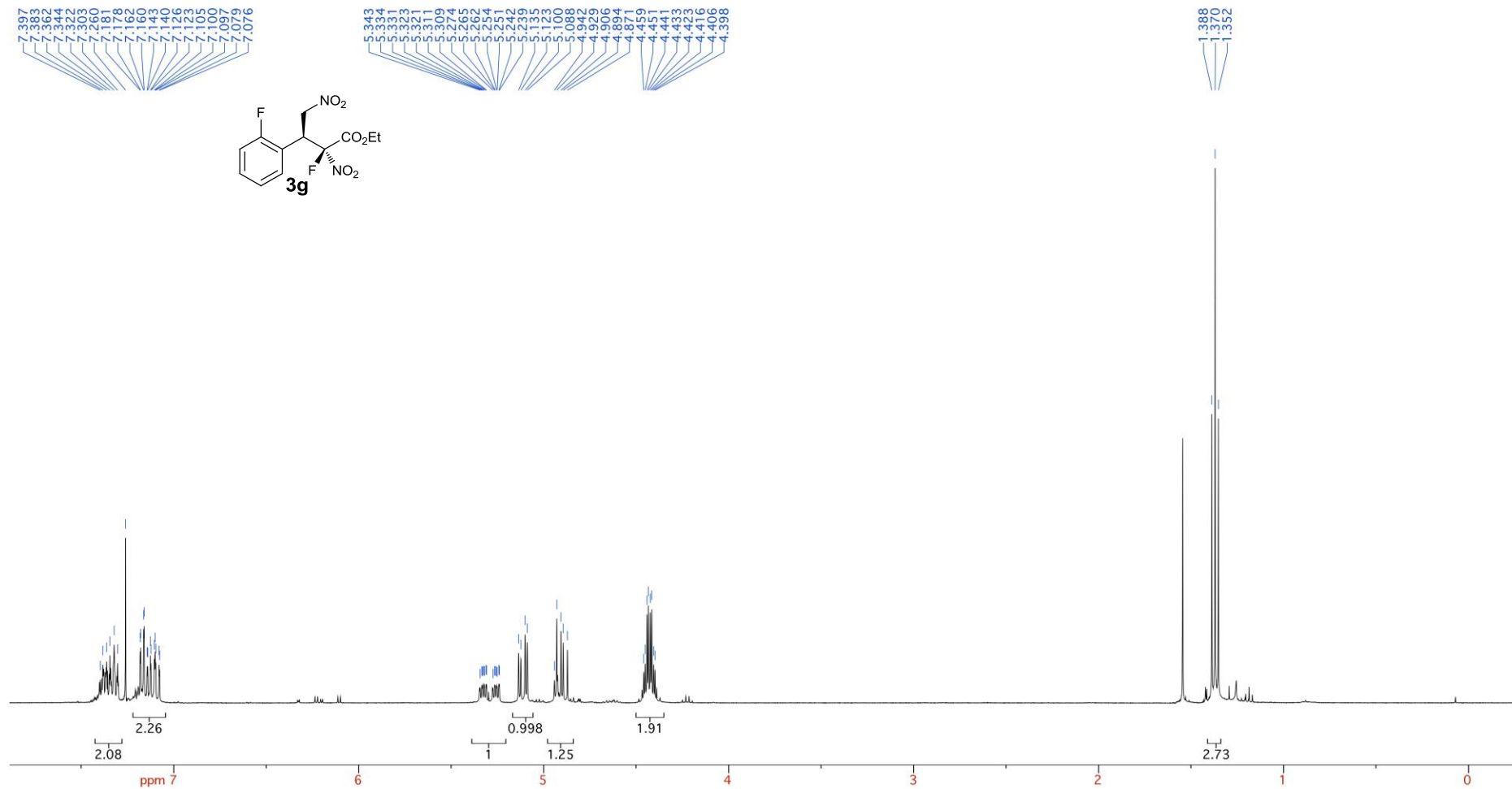
Major diastereomer (3f)

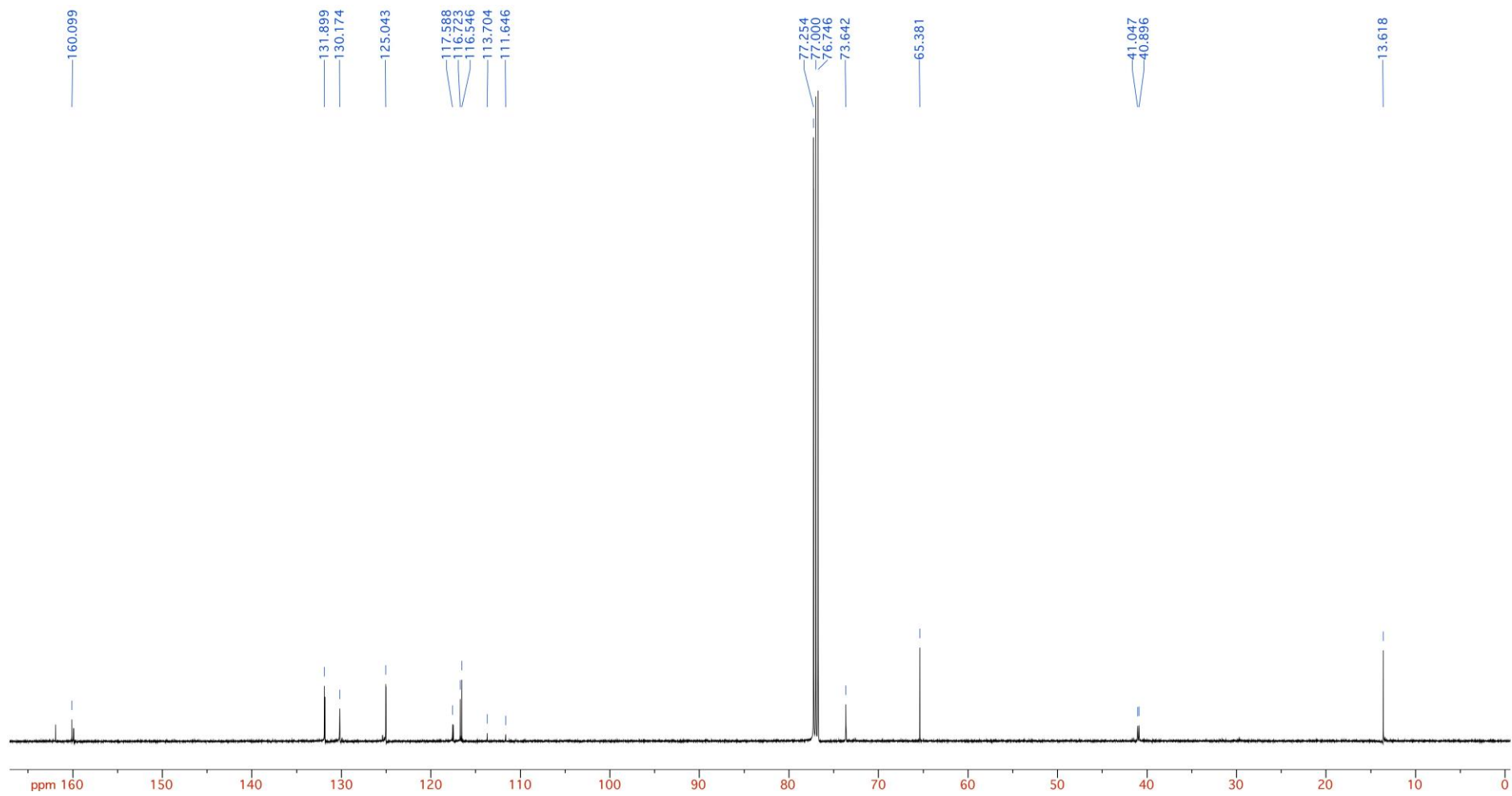


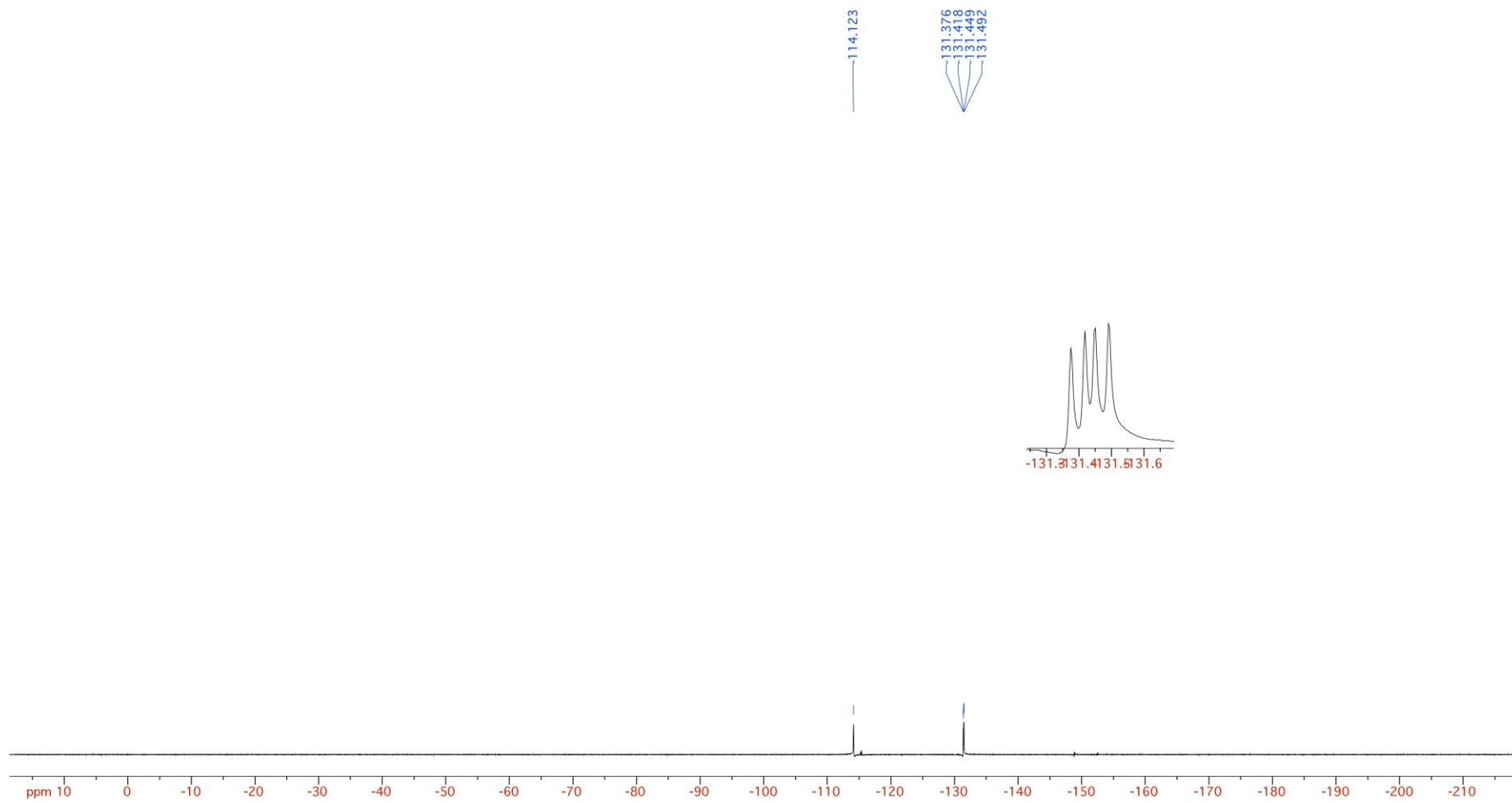




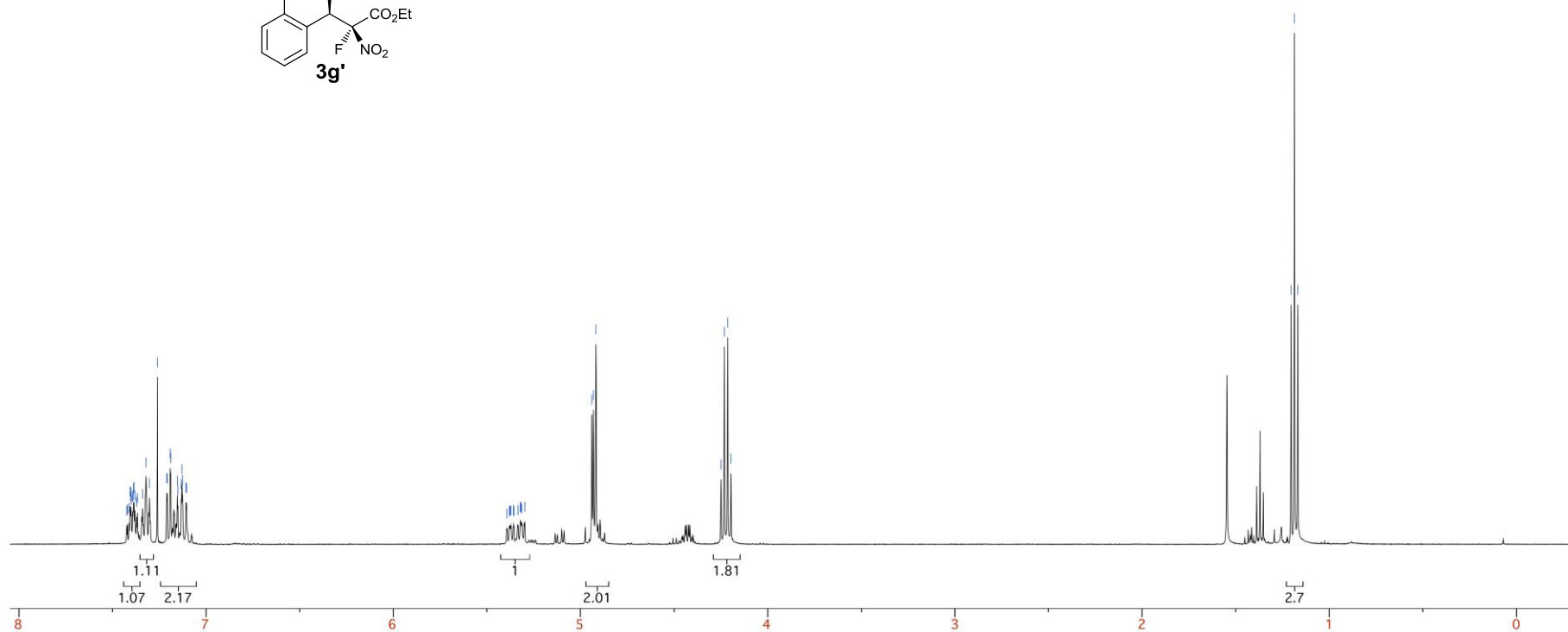
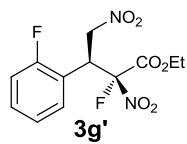
Major diastereomer (3g)

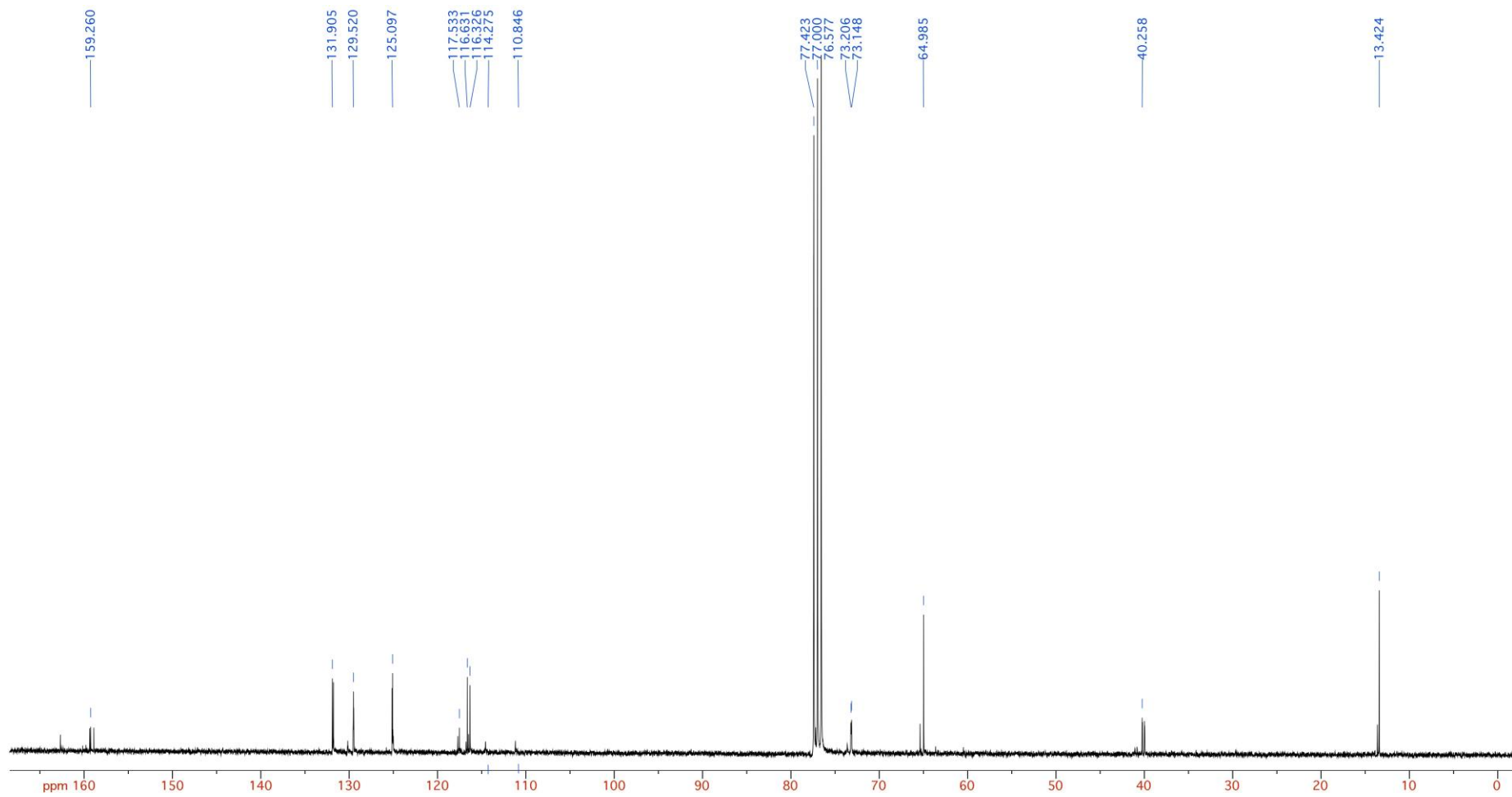


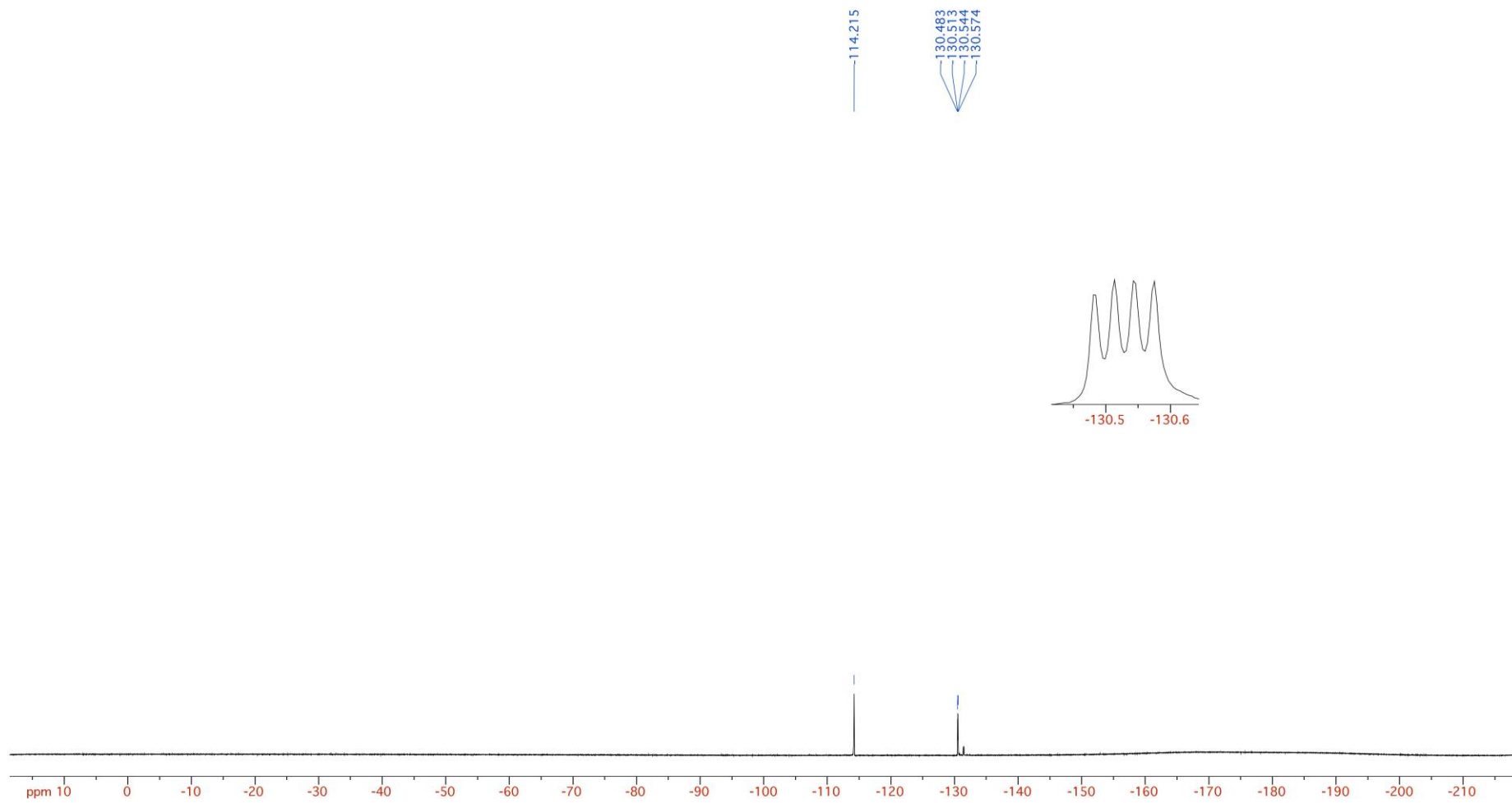




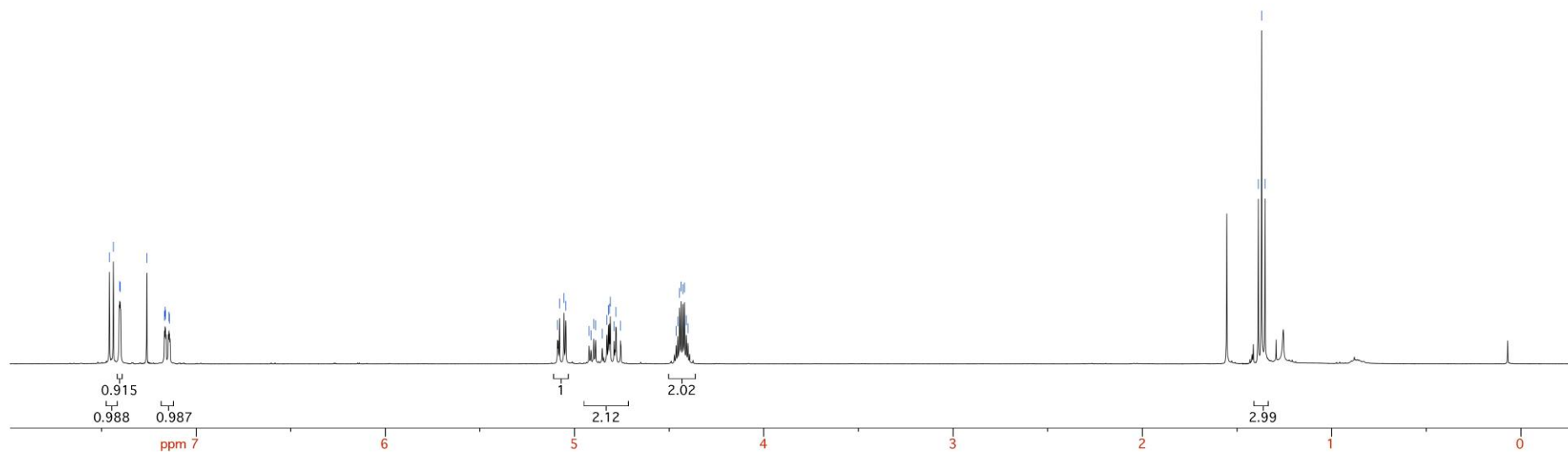
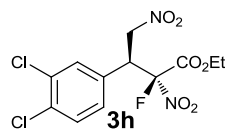
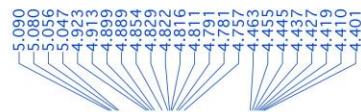
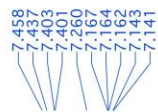
Minor diastereomer (3g', traces of major diastereomer)

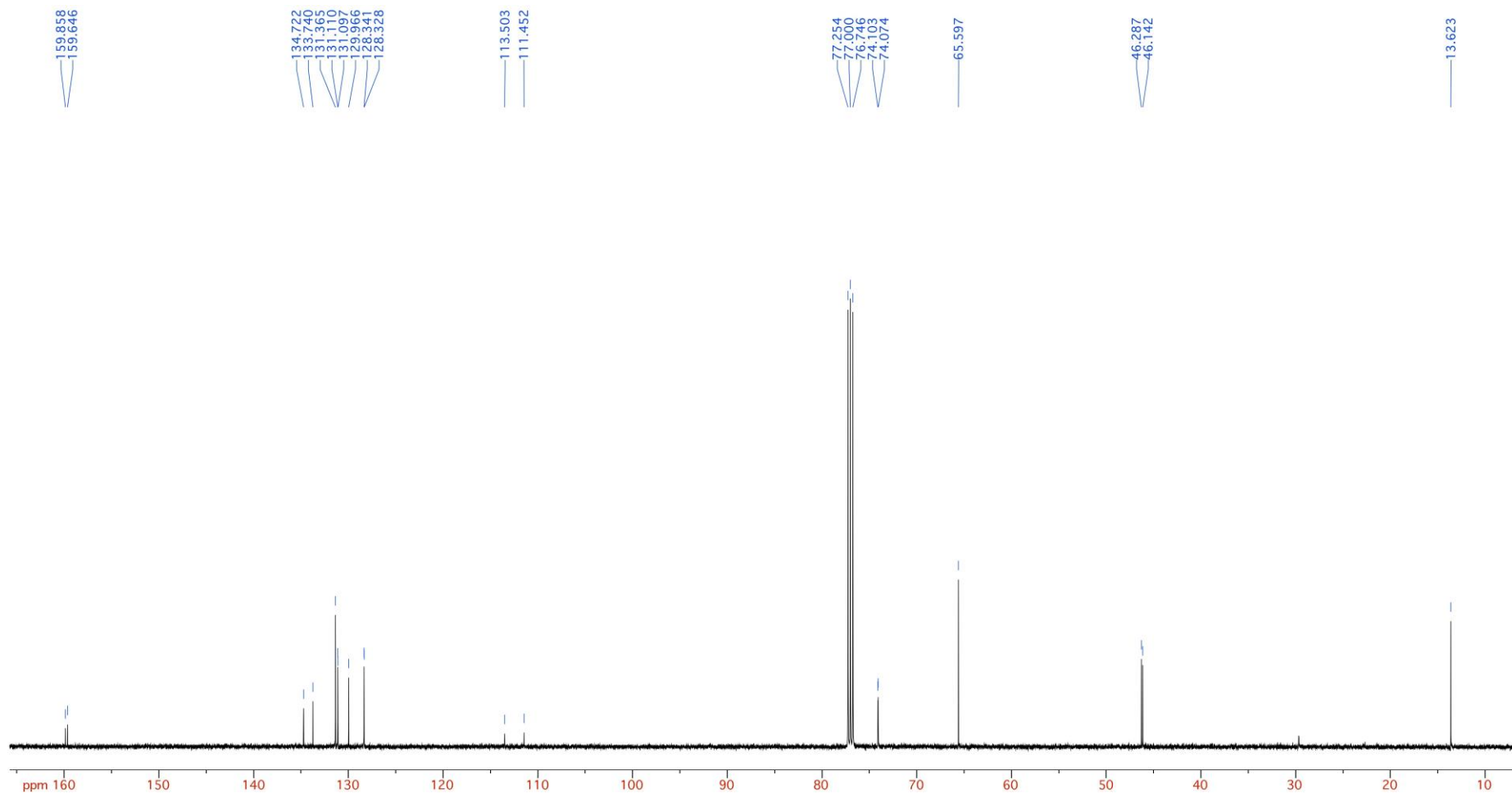


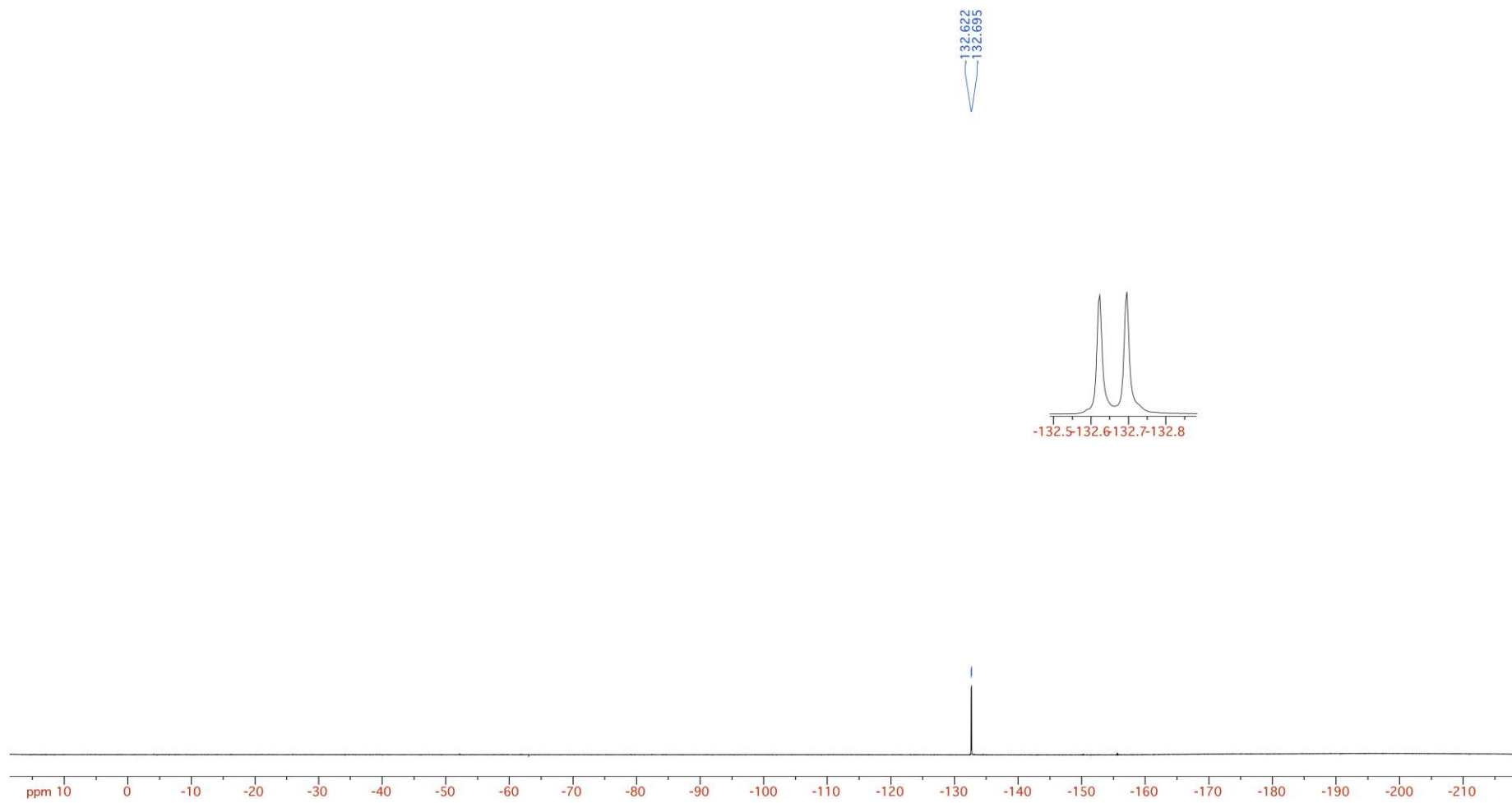




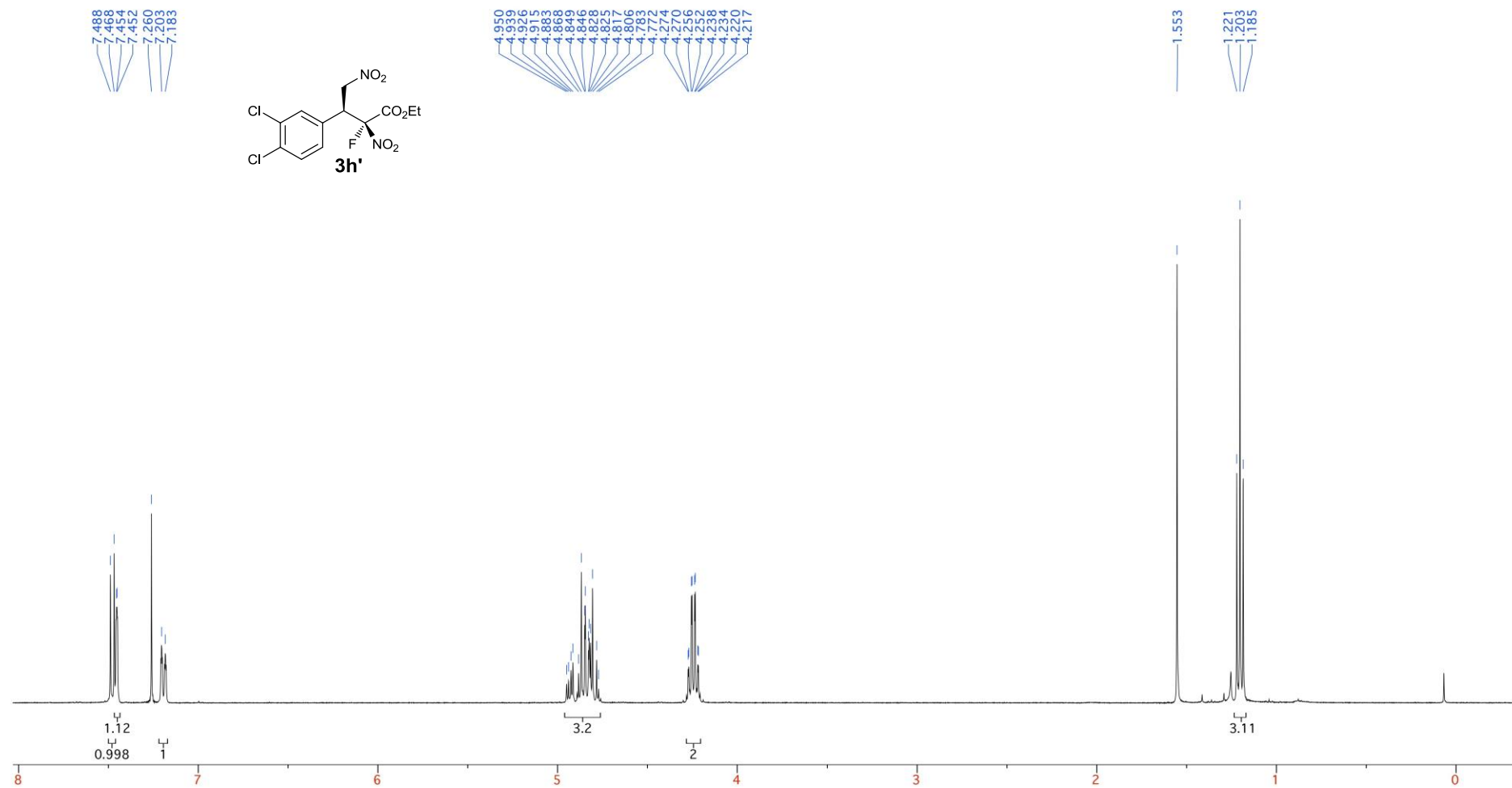
Major diastereomer (3h)

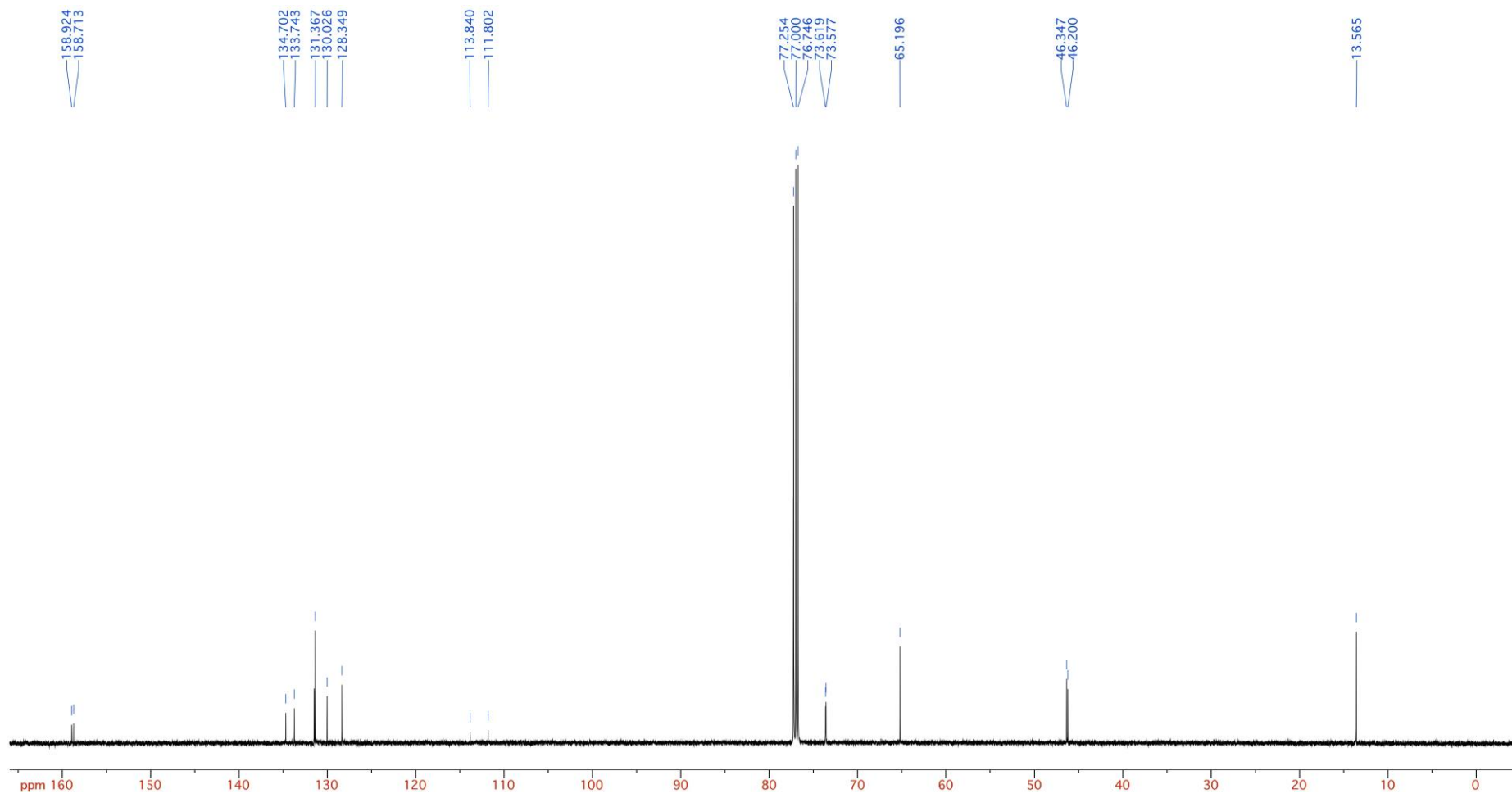


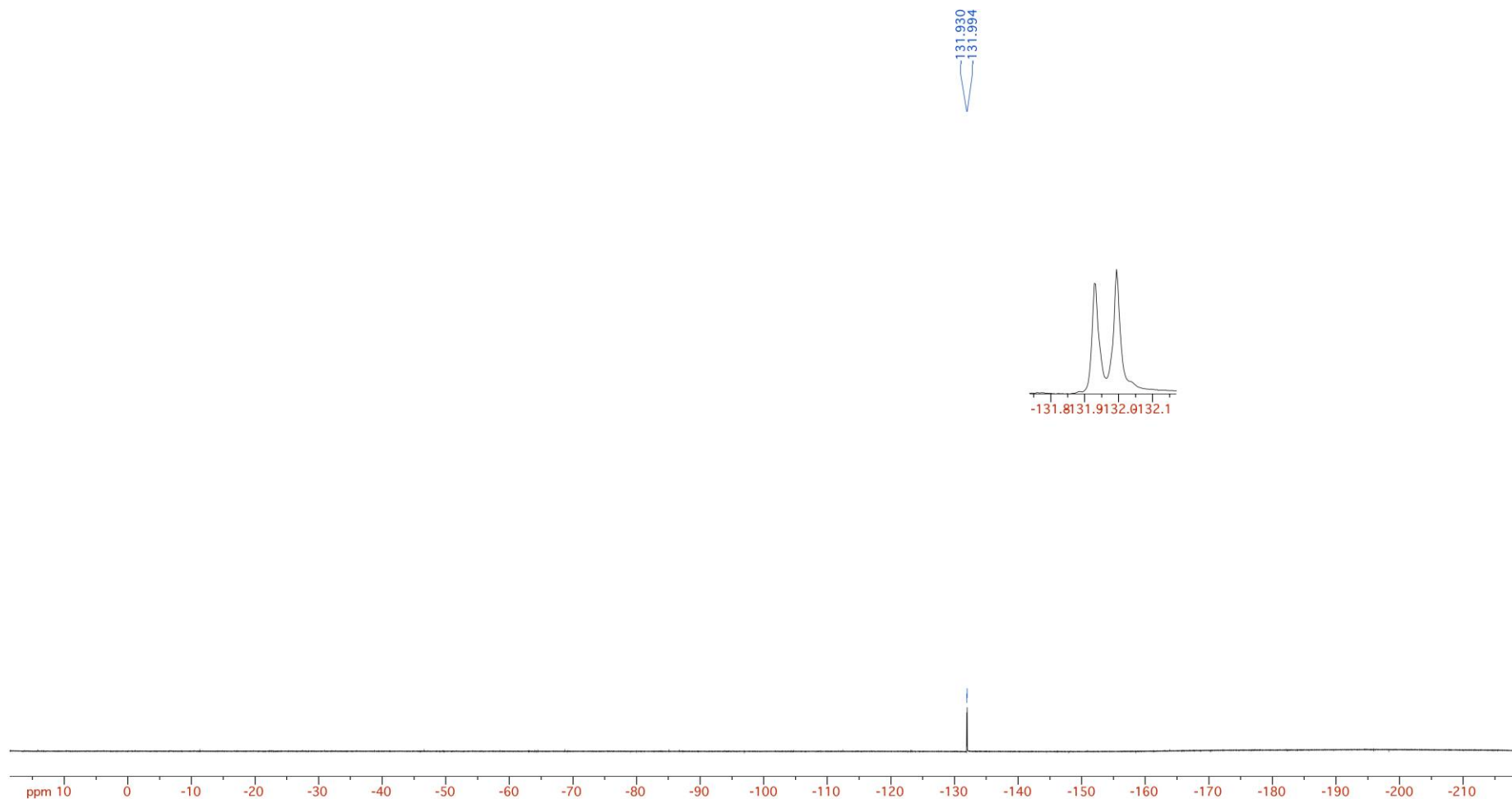




Minor diastereomer (3h')





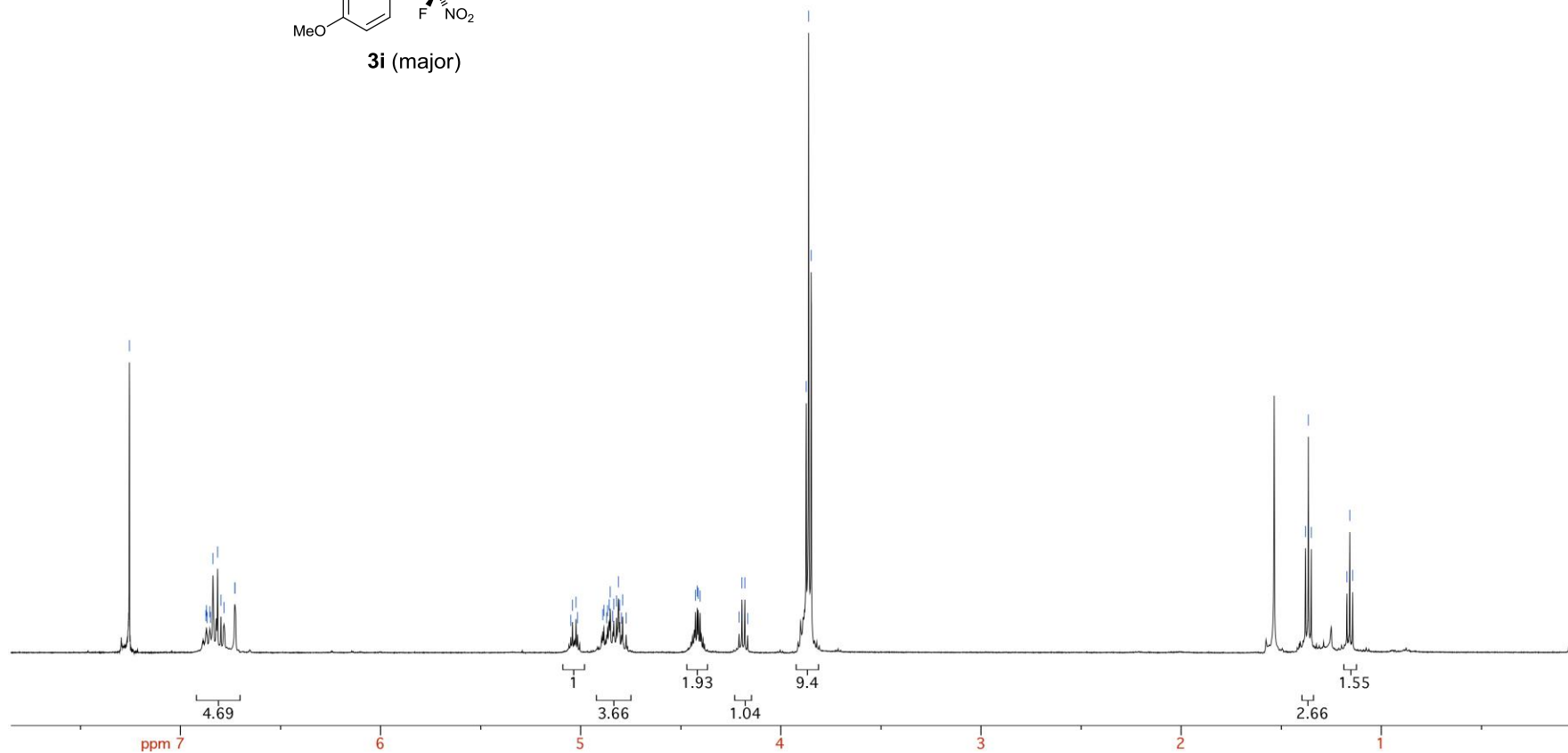
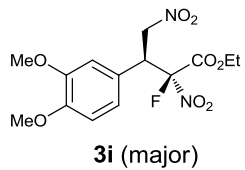


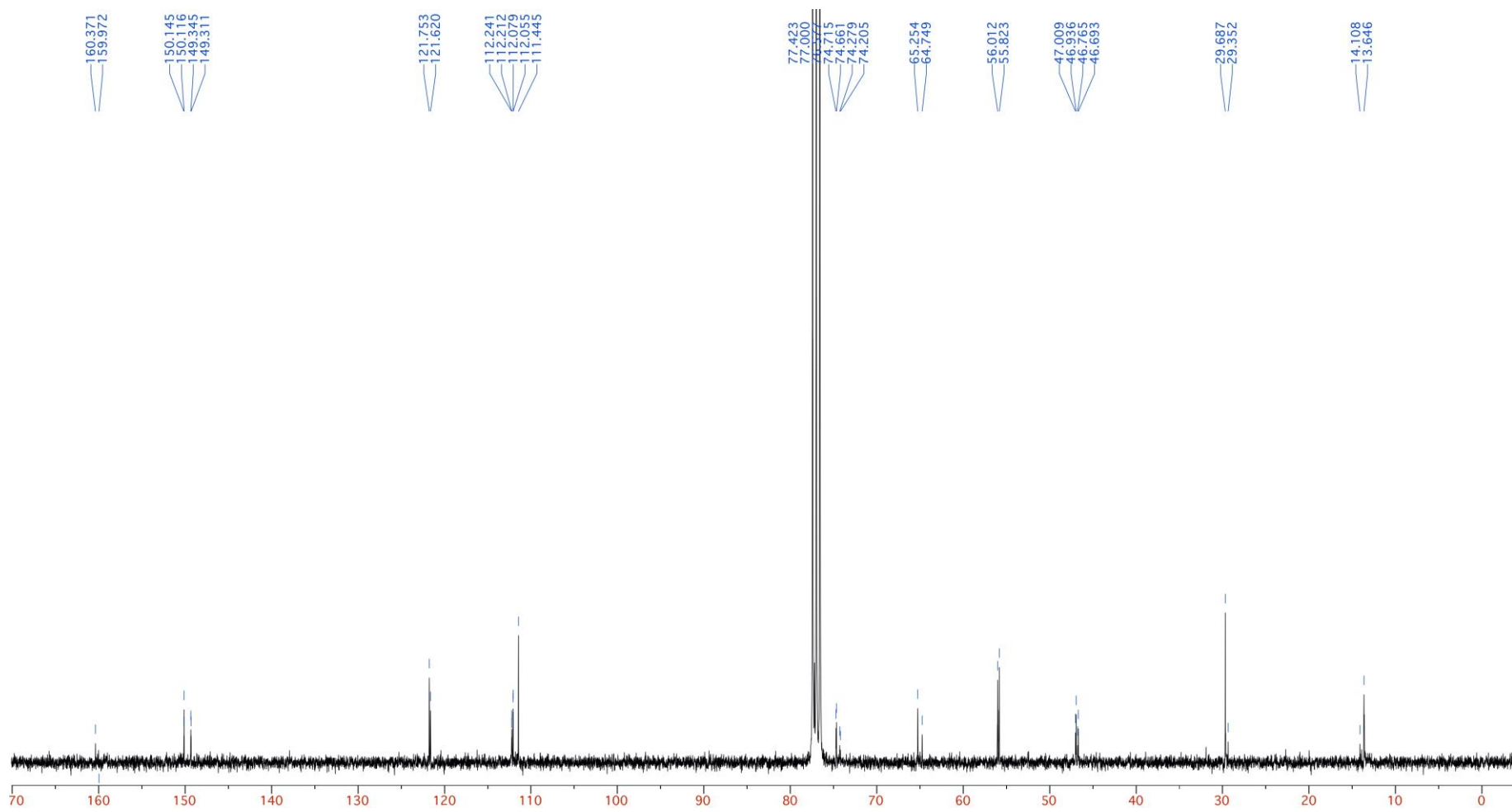
Diastereomeric mixture (3i)

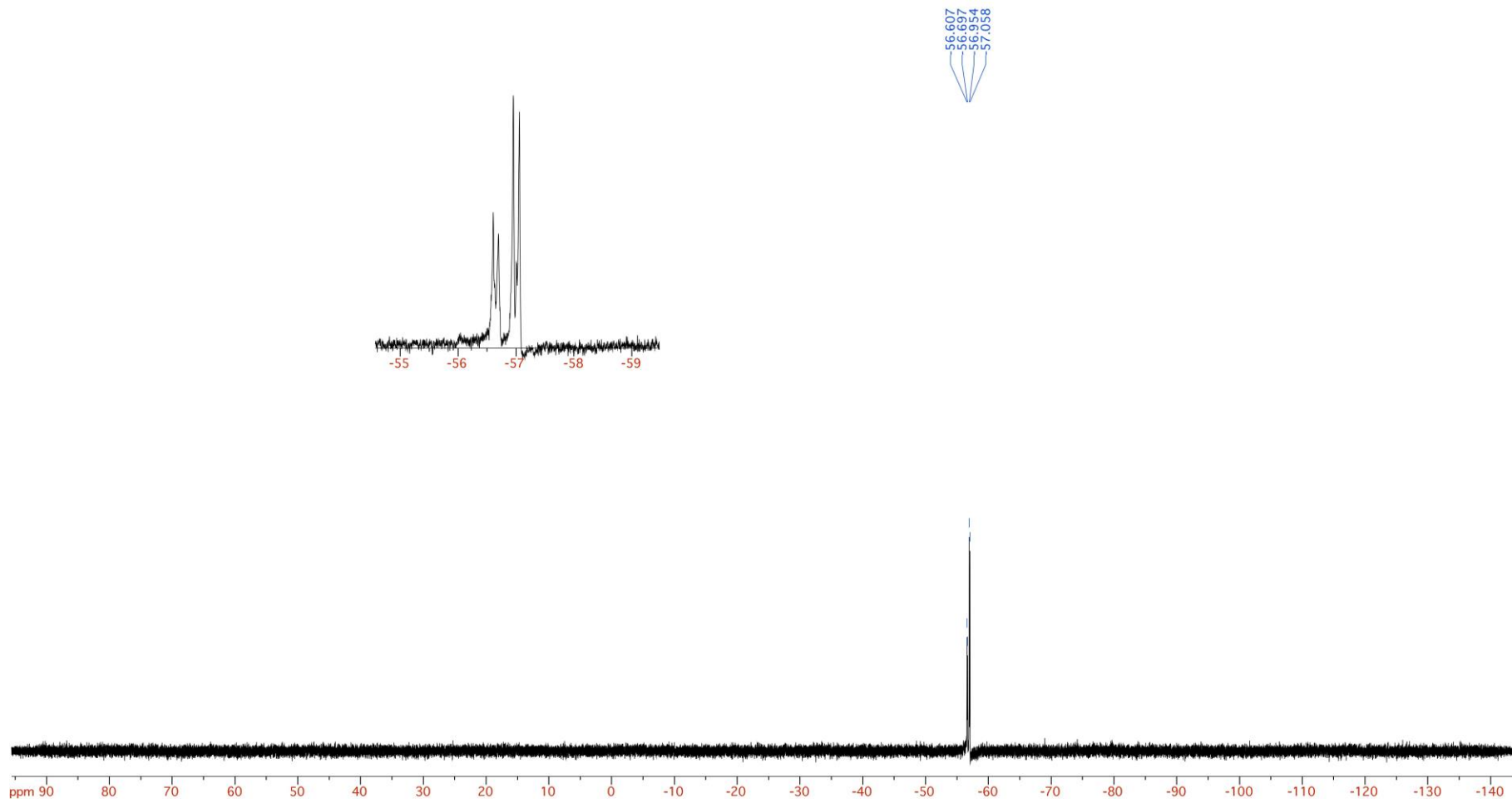
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6.850
6.838
6.814
6.798
6.782
6.728

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5.041
5.024
5.016
4.890
4.884
4.870
4.866
4.858
4.853
4.840
4.821
4.812
4.806
4.797
4.791
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3.848

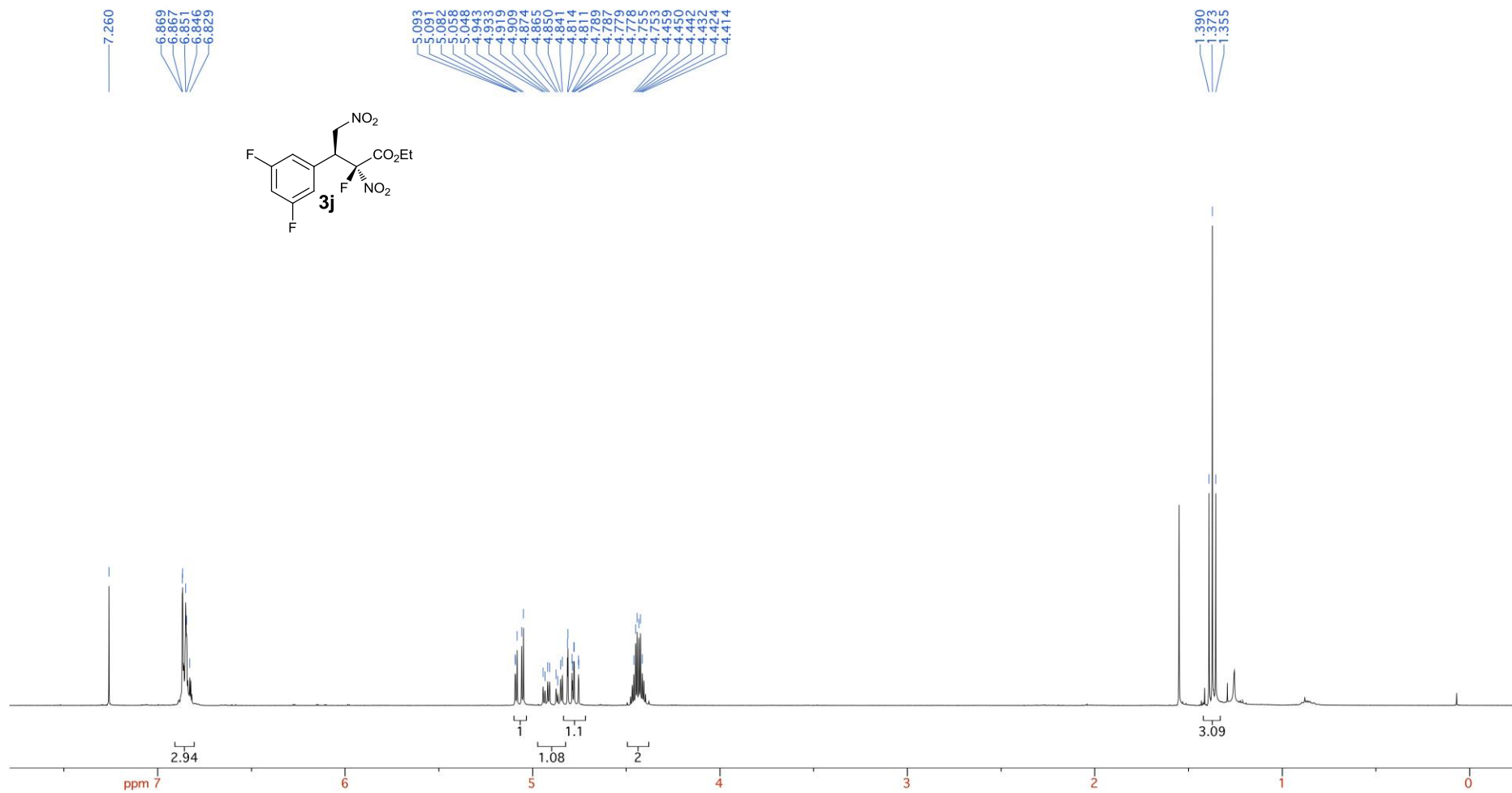
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1.158
1.143

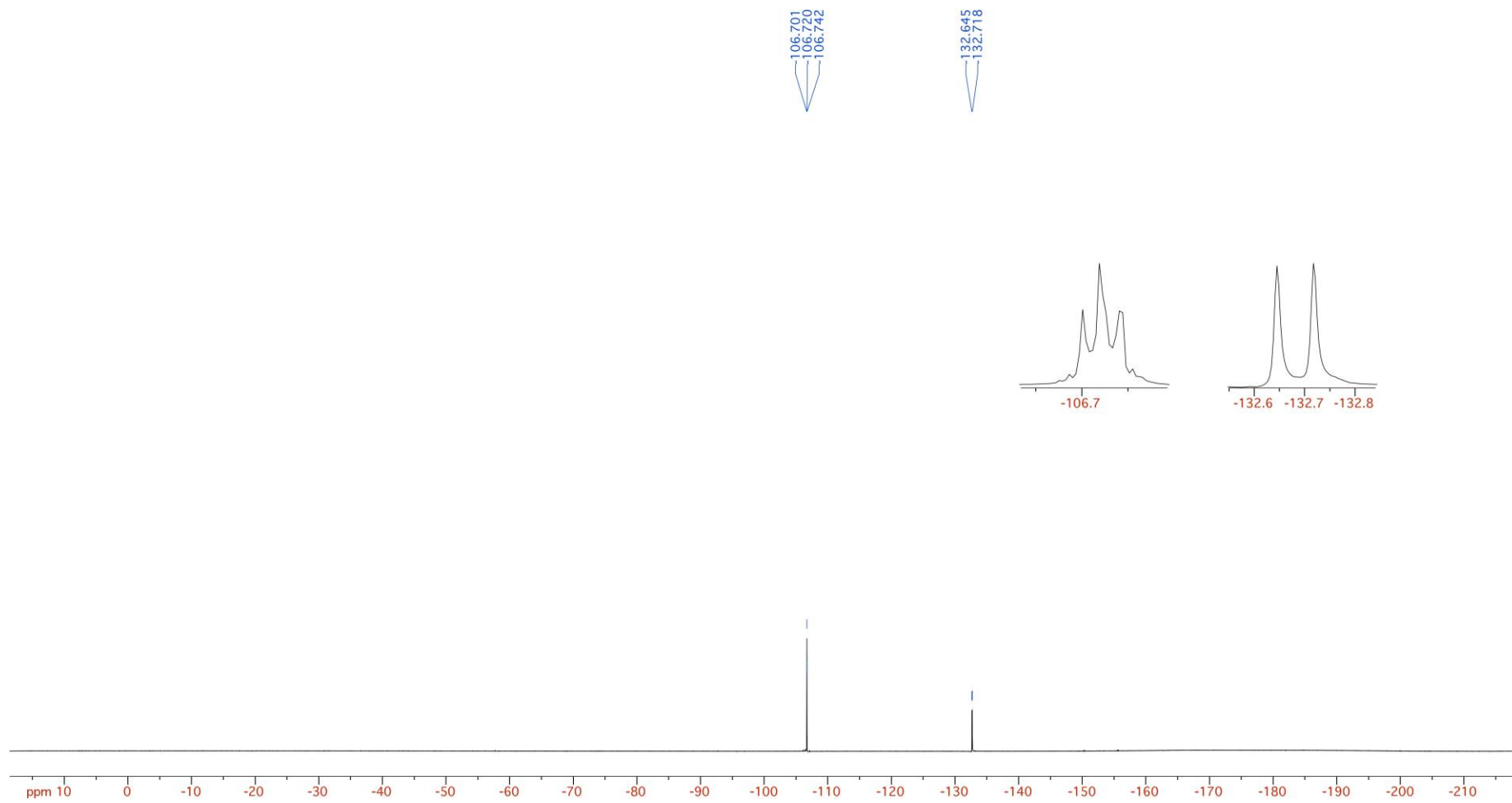


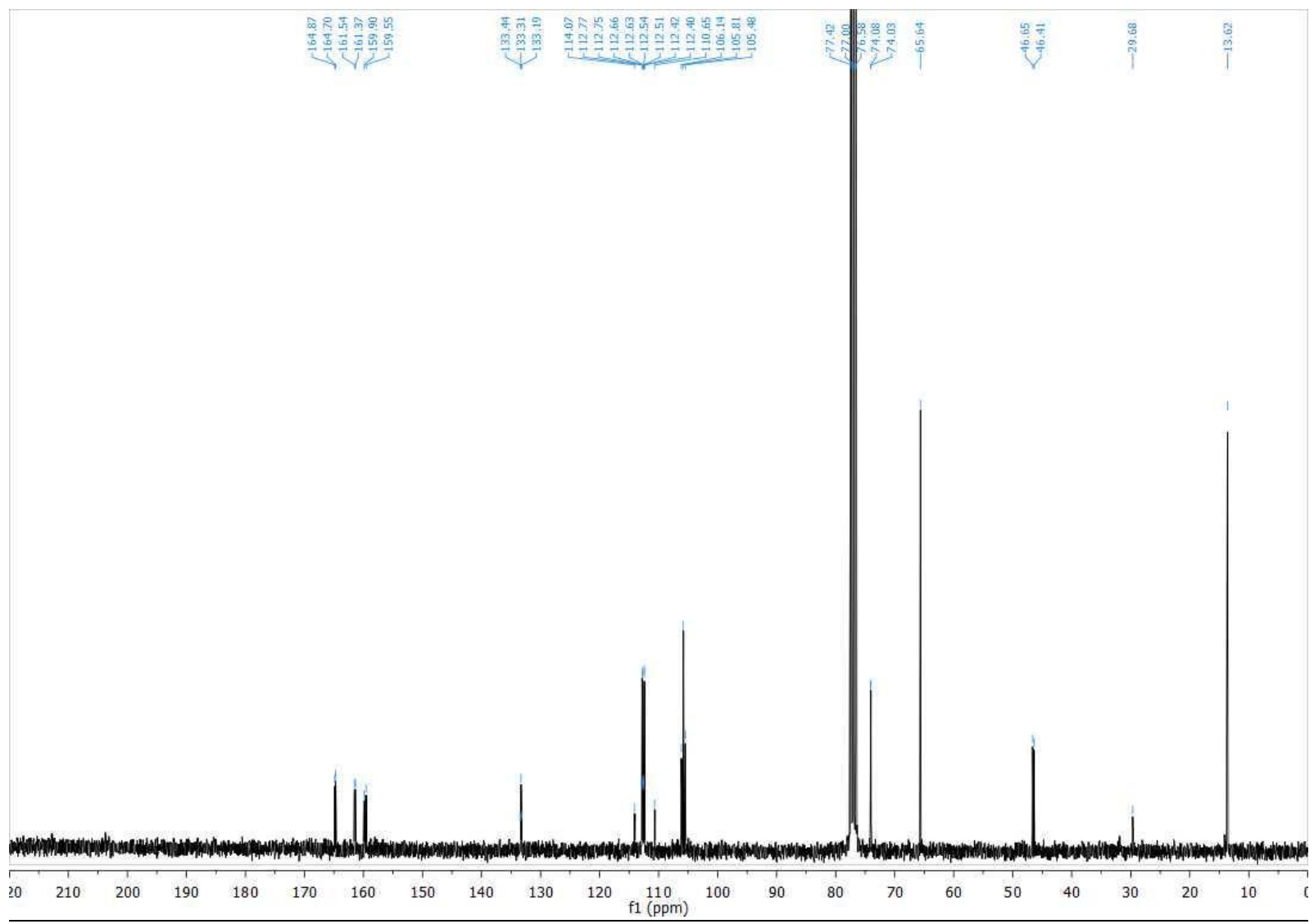




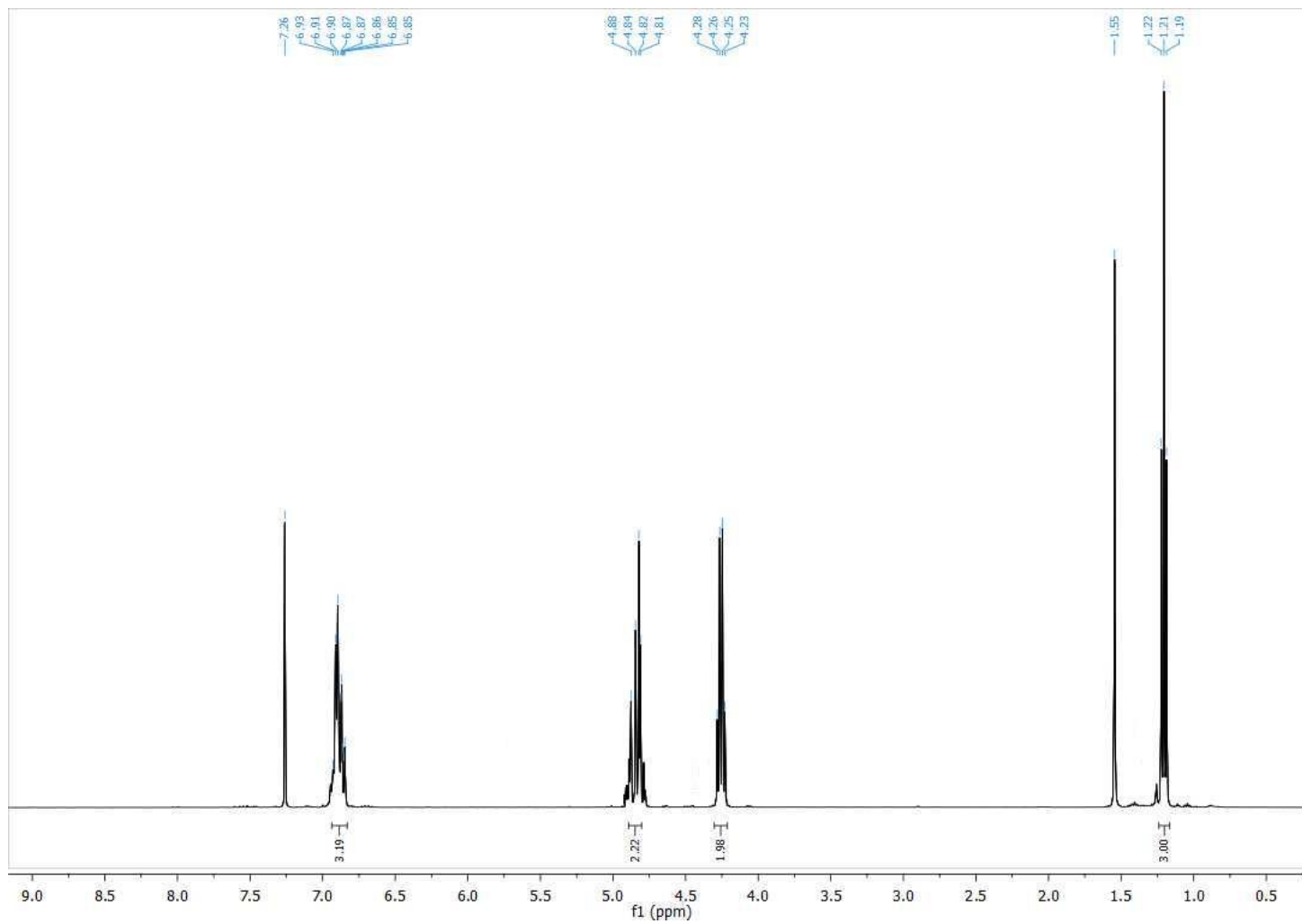
Major diastereomer (3j)

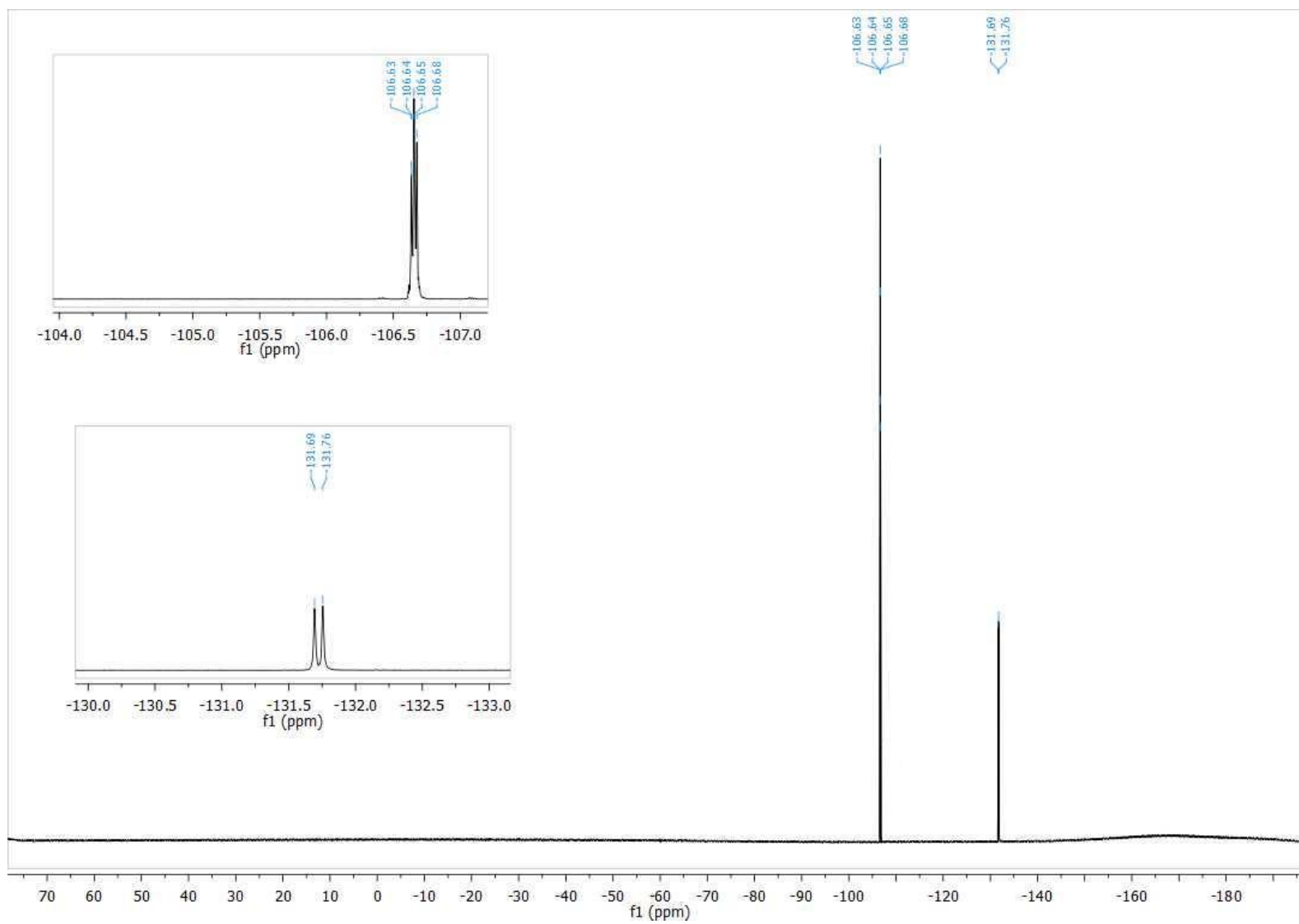


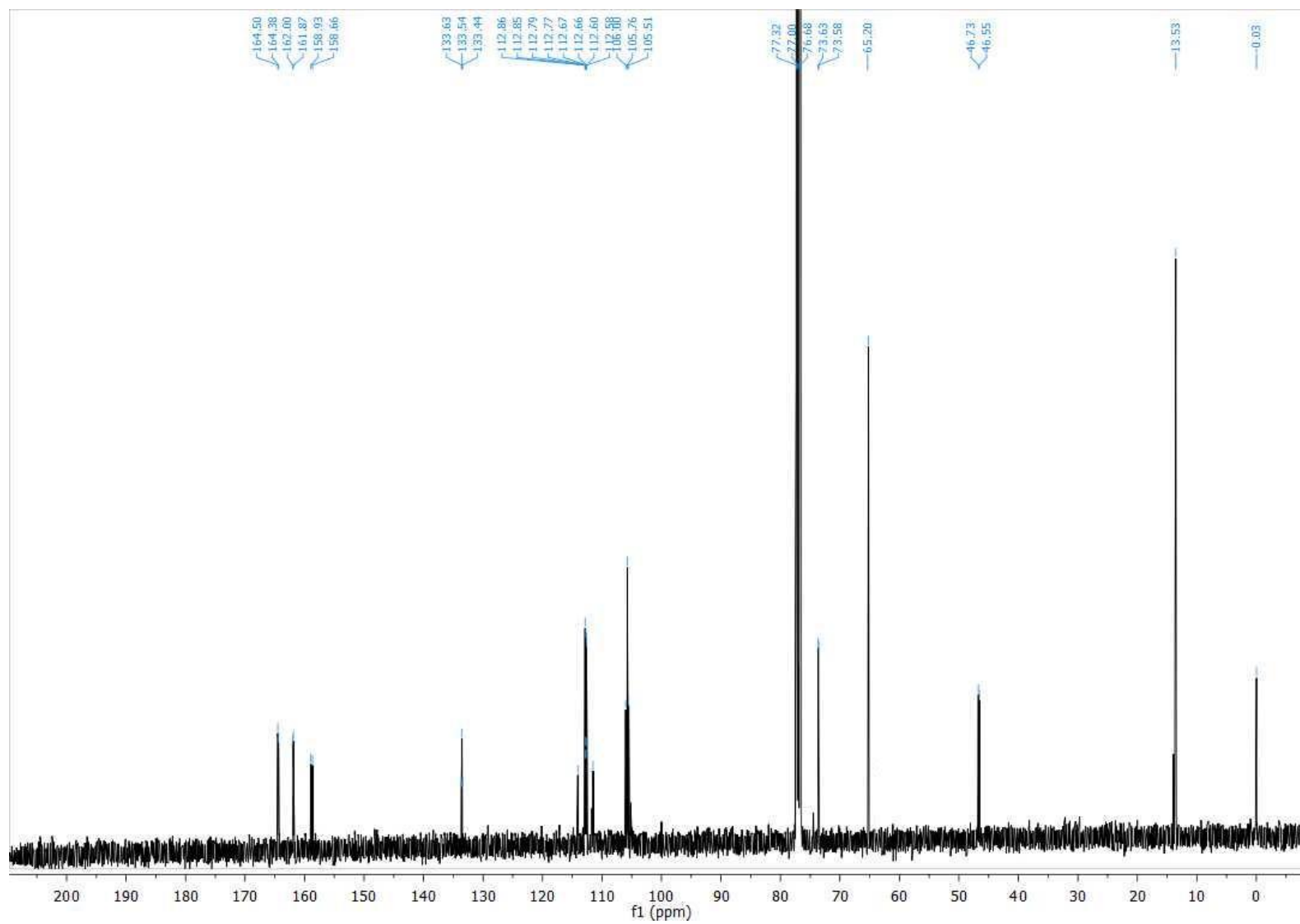




Minor diastereomer (3j)







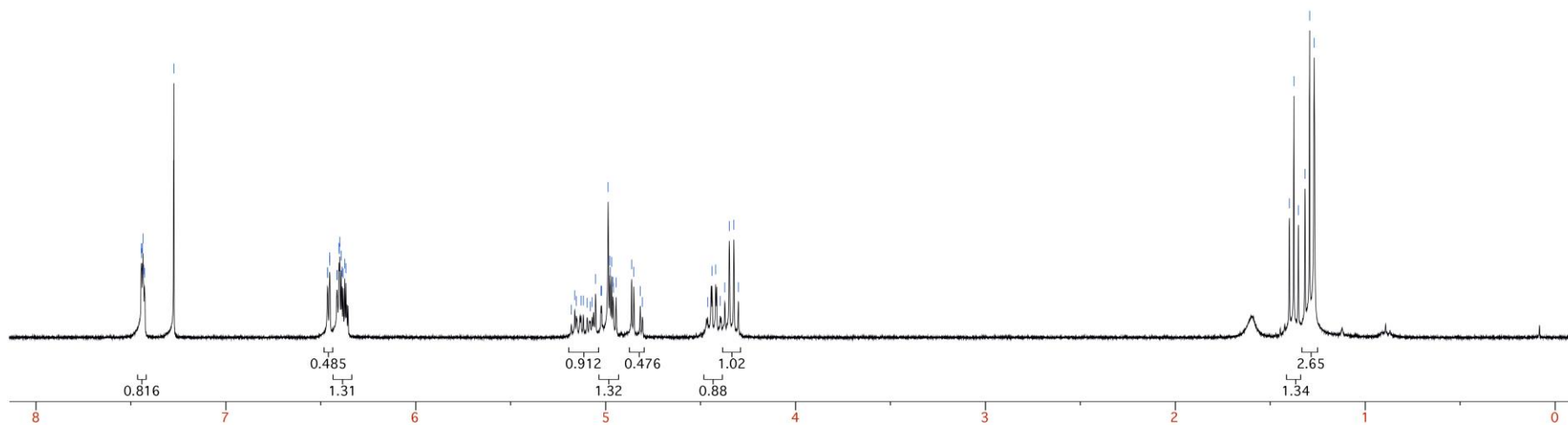
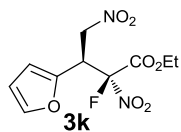
Diastereomeric mixture (3k)

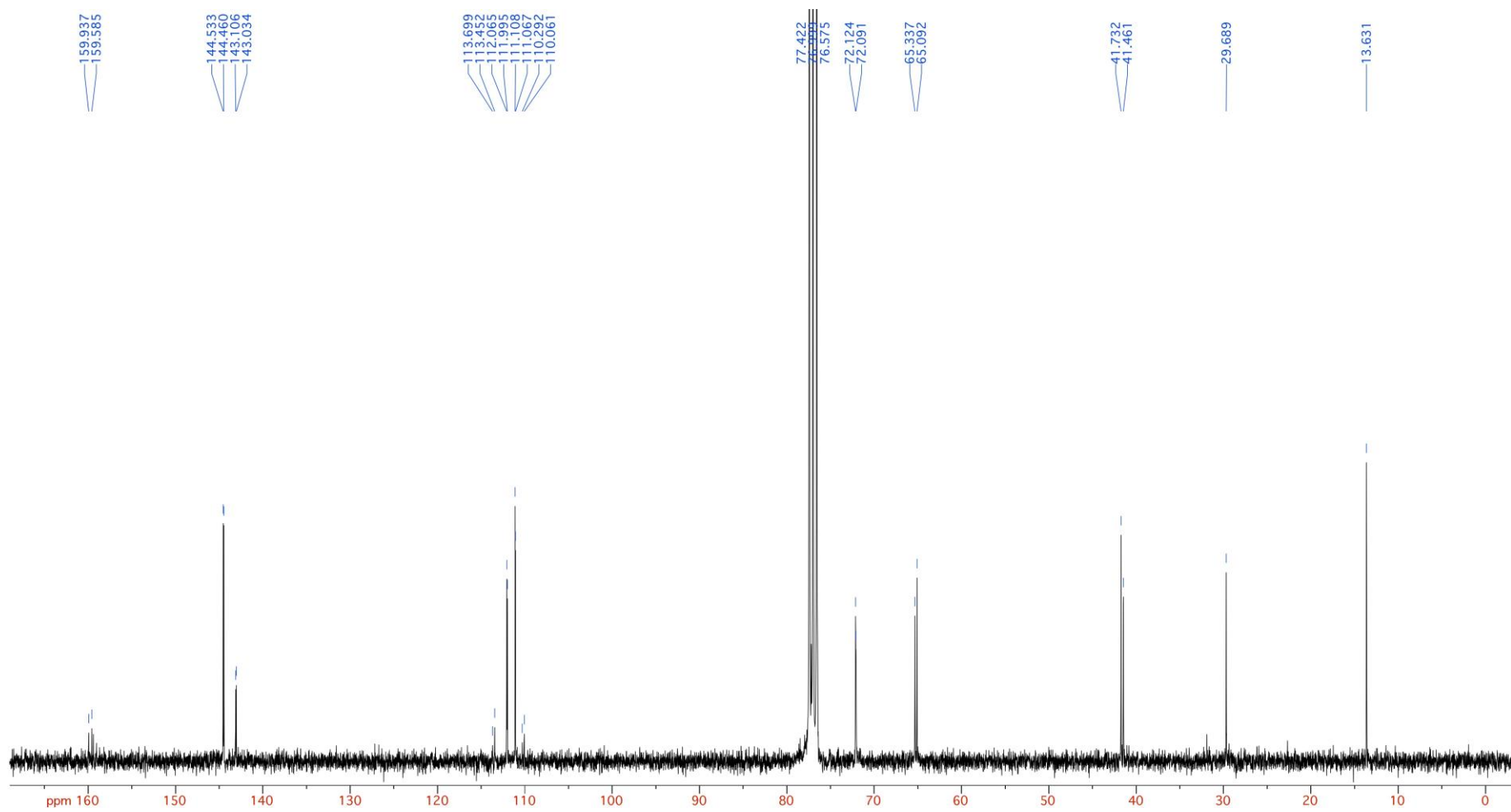
7.446
7.443
7.439
7.437
7.433
7.429
7.274

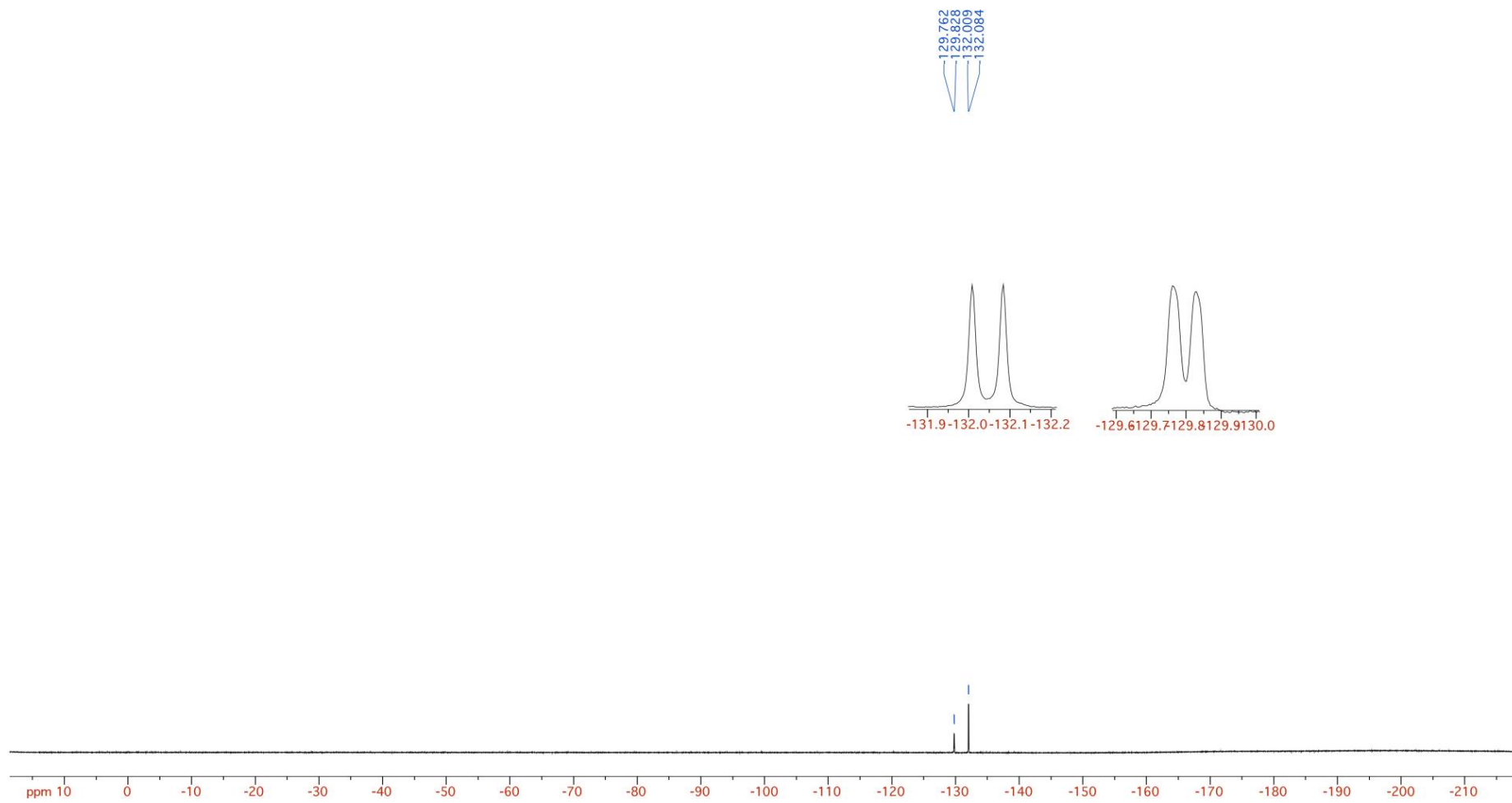
6.465
6.464
6.424
6.415
6.414
6.404
6.403
6.393
6.388
6.392
6.368

5.181
5.162
5.154
5.130
5.118
5.087
5.071
5.053
5.024
5.022
4.987
4.978
4.976
4.969
4.960
4.945
4.863
4.852
4.818
4.807
4.465
4.429
4.397
4.373
4.349
4.325
4.301

1.899
1.859
1.817
1.293
1.269

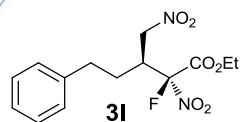




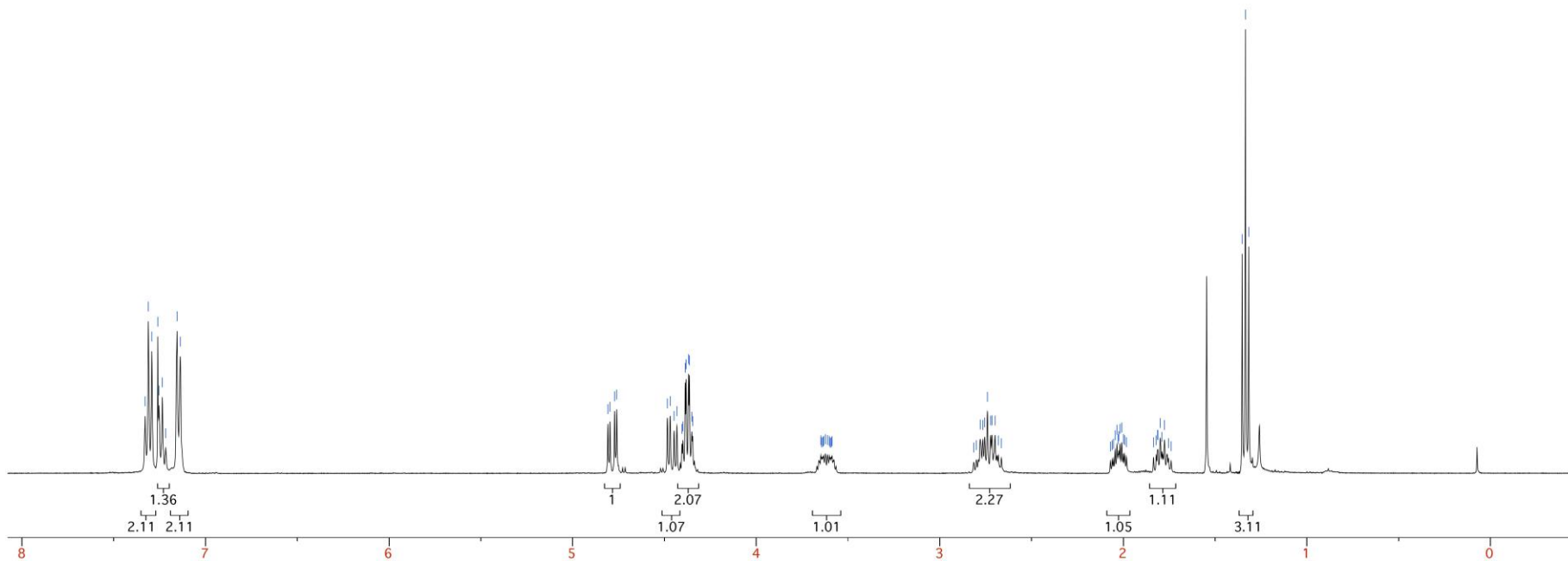


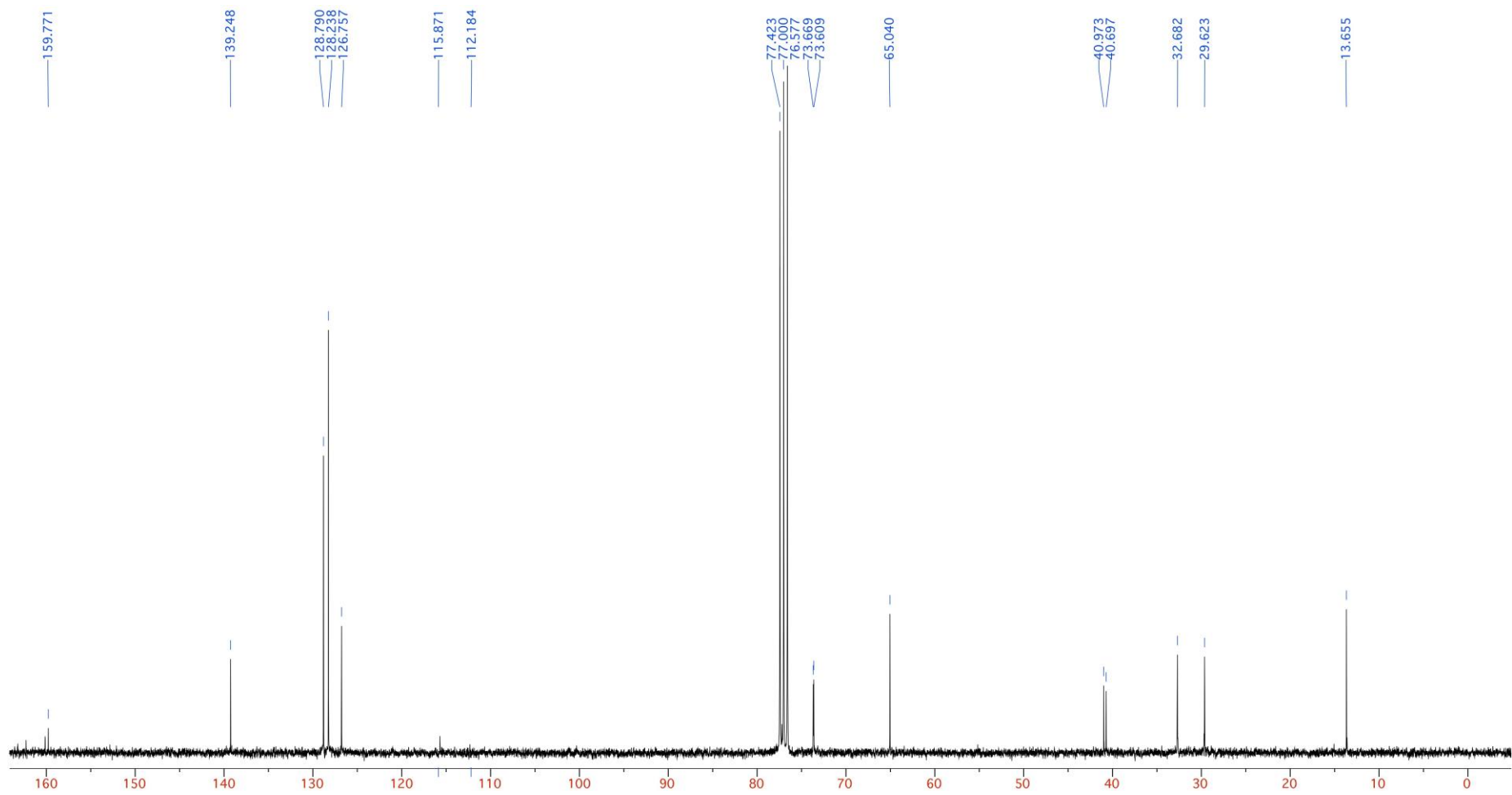
Major diastereomer (31)

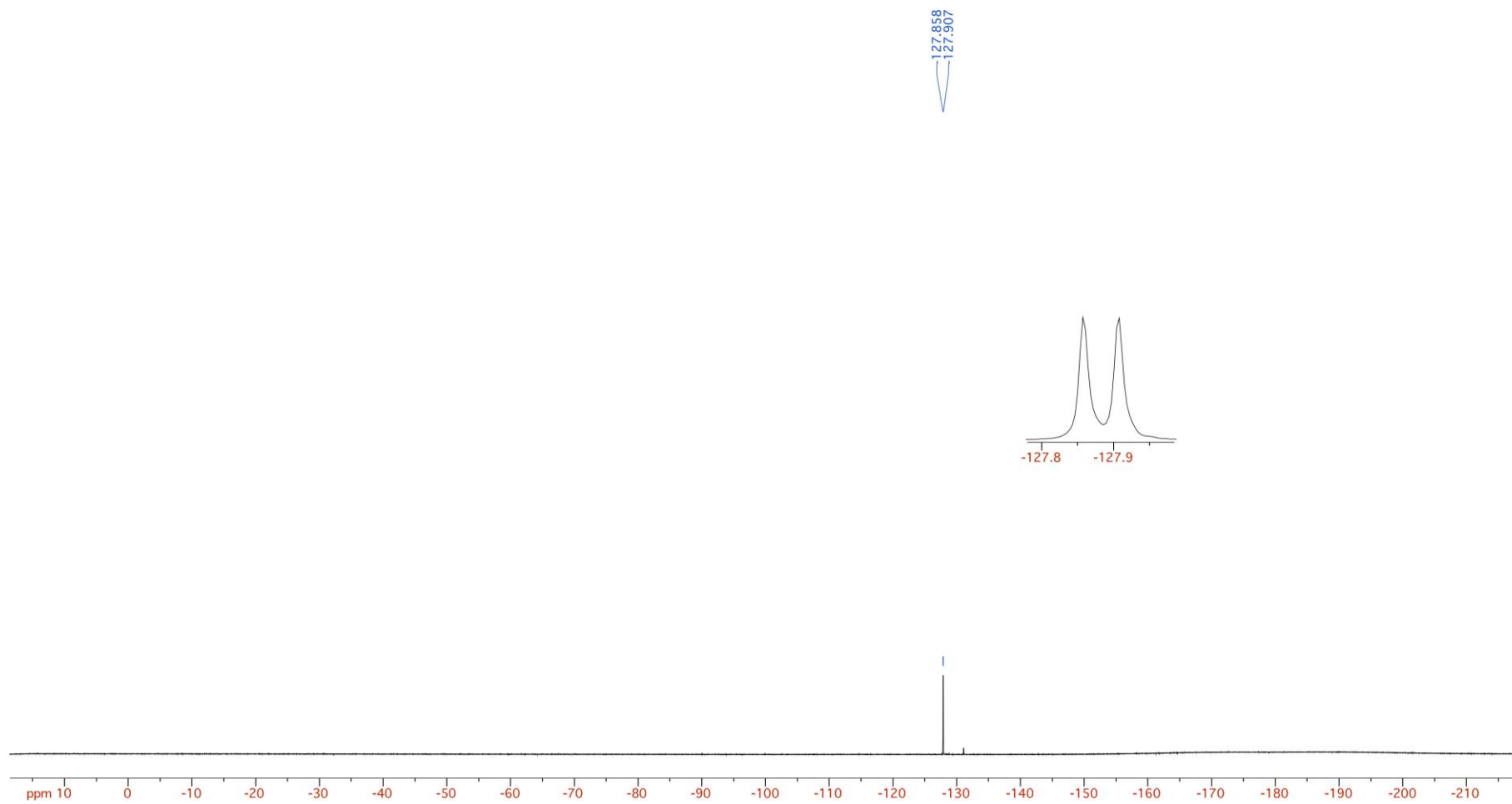
7.317
7.292
7.265
7.240
7.215
7.189
7.164
7.139



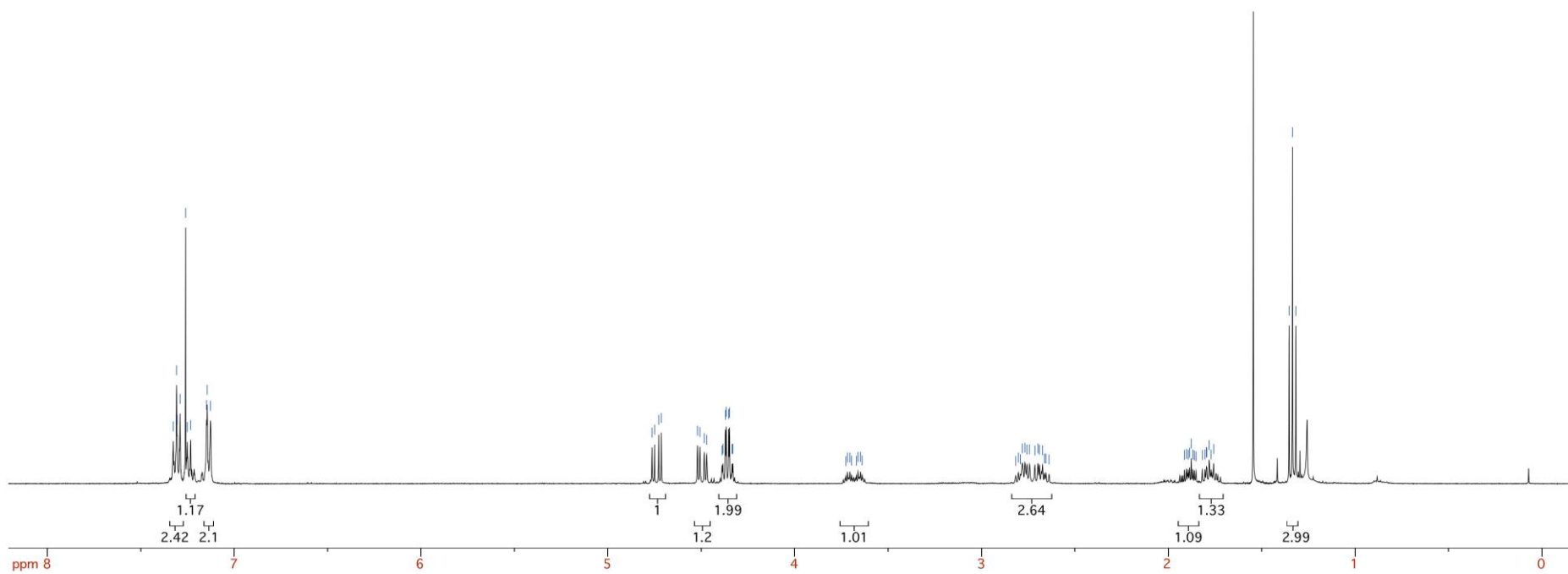
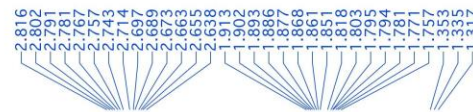
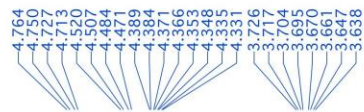
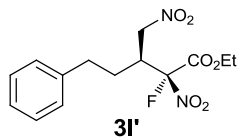
4.808
4.796
4.779
4.760
4.749
4.737
4.725
4.713
4.699
4.687
4.675
4.663
4.651
4.639
4.627
4.615
4.603
4.591
4.579
4.567
4.555
4.543
4.531
4.519
4.507
4.495
4.483
4.471
4.459
4.447
4.435
4.423
4.411
4.399
4.387
4.375
4.363
4.351
4.339
4.327
4.315
4.303
4.291
4.279
4.267
4.255
4.243
4.231
4.219
4.207
4.195
4.183
4.171
4.159
4.147
4.135
4.123
4.111
4.099
4.087
4.075
4.063
4.051
4.039
4.027
4.015
4.003
3.991
3.979
3.967
3.955
3.943
3.931
3.919
3.907
3.895
3.883
3.871
3.859
3.847
3.835
3.823
3.811
3.799
3.787
3.775
3.763
3.751
3.739
3.727
3.715
3.703
3.691
3.679
3.667
3.655
3.643
3.631
3.619
3.607
3.595
3.583
3.571
3.559
3.547
3.535
3.523
3.511
3.499
3.487
3.475
3.463
3.451
3.439
3.427
3.415
3.403
3.391
3.379
3.367
3.355
3.343
3.331
3.319
3.307
3.295
3.283
3.271
3.259
3.247
3.235
3.223
3.211
3.199
3.187
3.175
3.163
3.151
3.139
3.127
3.115
3.103
3.091
3.079
3.067
3.055
3.043
3.031
3.019
3.007
2.995
2.983
2.971
2.959
2.947
2.935
2.923
2.911
2.899
2.887
2.875
2.863
2.851
2.839
2.827
2.815
2.803
2.791
2.779
2.767
2.755
2.743
2.731
2.719
2.707
2.695
2.683
2.671
2.659
2.647
2.635
2.623
2.611
2.599
2.587
2.575
2.563
2.551
2.539
2.527
2.515
2.503
2.491
2.479
2.467
2.455
2.443
2.431
2.419
2.407
2.395
2.383
2.371
2.359
2.347
2.335
2.323
2.311
2.299
2.287
2.275
2.263
2.251
2.239
2.227
2.215
2.203
2.191
2.179
2.167
2.155
2.143
2.131
2.119
2.107
2.095
2.083
2.071
2.059
2.047
2.035
2.023
2.011
2.000
1.988
1.976
1.964
1.952
1.940
1.928
1.916
1.904
1.892
1.880
1.868
1.856
1.844
1.832
1.820
1.808
1.796
1.784
1.772
1.760
1.748
1.736
1.724
1.712
1.700
1.688
1.676
1.664
1.652
1.640
1.628
1.616
1.604
1.592
1.580
1.568
1.556
1.544
1.532
1.520
1.508
1.496
1.484
1.472
1.460
1.448
1.436
1.424
1.412
1.400
1.388
1.376
1.364
1.352
1.340
1.328
1.316
1.304
1.292
1.280
1.268
1.256
1.244
1.232
1.220
1.208
1.196
1.184
1.172
1.160
1.148
1.136
1.124
1.112
1.100
1.088
1.076
1.064
1.052
1.040
1.028
1.016
1.004
0.992
0.980
0.968
0.956
0.944
0.932
0.920
0.908
0.896
0.884
0.872
0.860
0.848
0.836
0.824
0.812
0.800
0.788
0.776
0.764
0.752
0.740
0.728
0.716
0.704
0.692
0.680
0.668
0.656
0.644
0.632
0.620
0.608
0.596
0.584
0.572
0.560
0.548
0.536
0.524
0.512
0.500
0.488
0.476
0.464
0.452
0.440
0.428
0.416
0.404
0.392
0.380
0.368
0.356
0.344
0.332
0.320
0.308
0.296
0.284
0.272
0.260
0.248
0.236
0.224
0.212
0.200
0.188
0.176
0.164
0.152
0.140
0.128
0.116
0.104
0.092
0.080
0.068
0.056
0.044
0.032
0.020
0.008
0.000

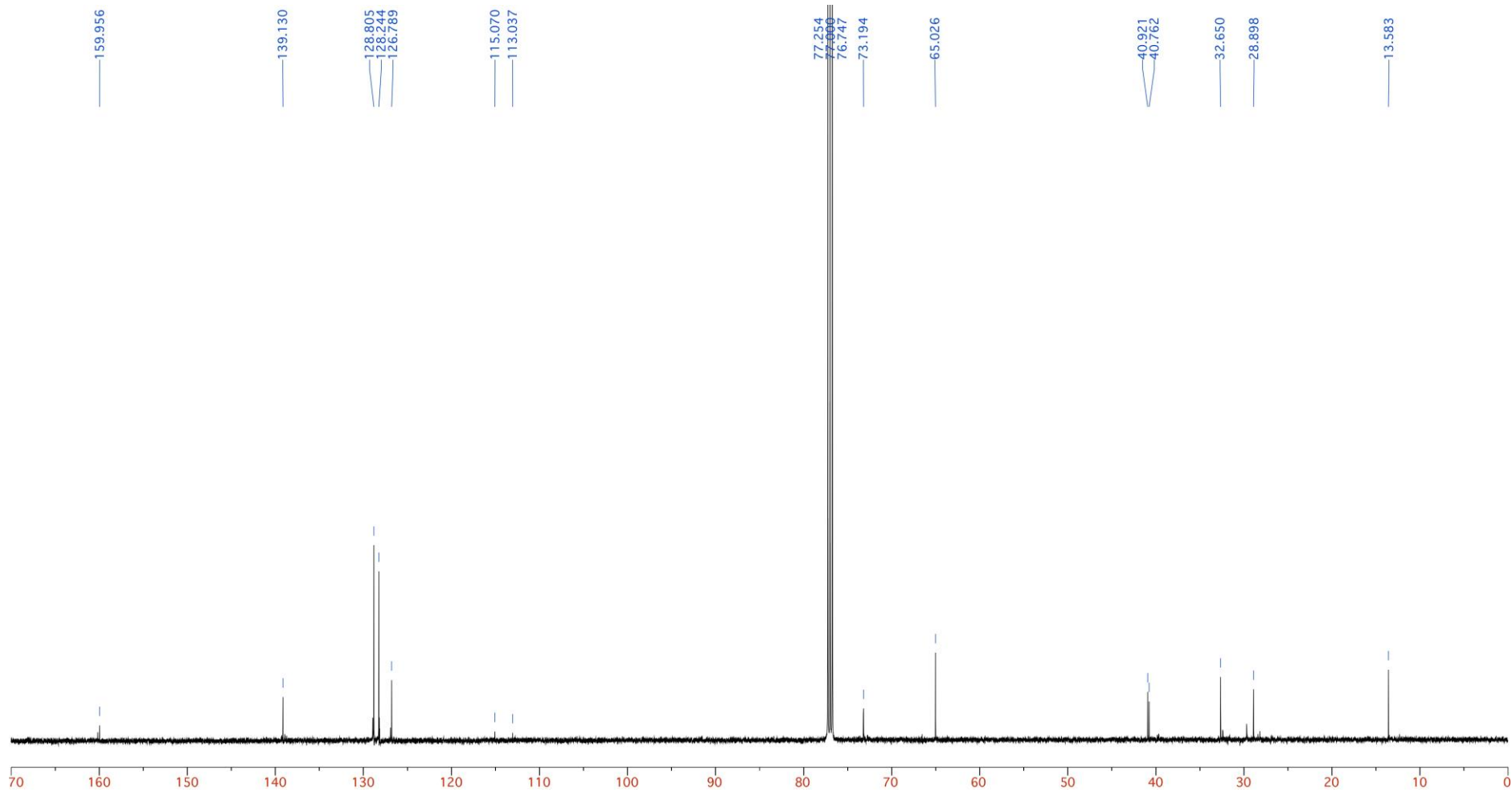


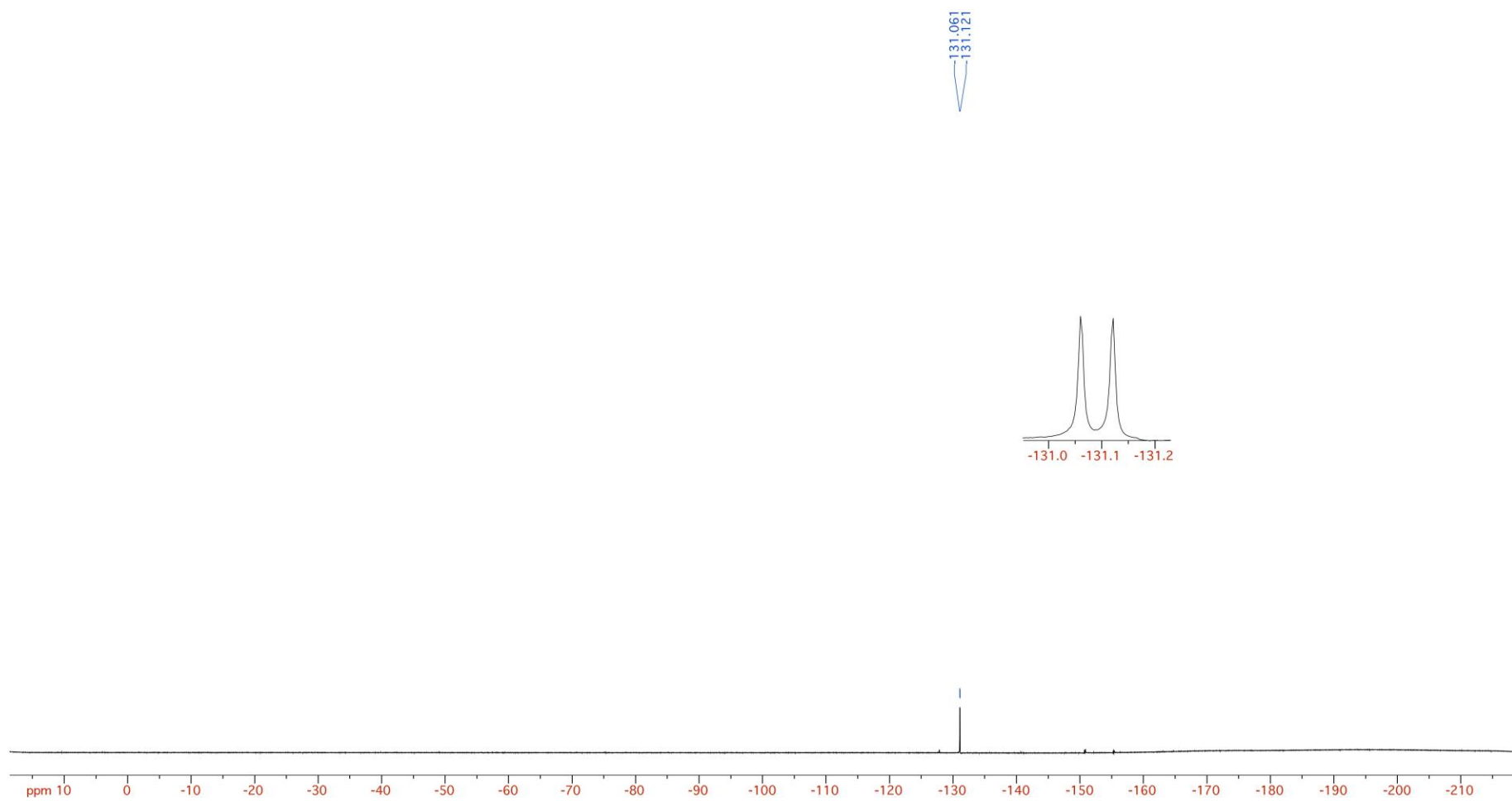




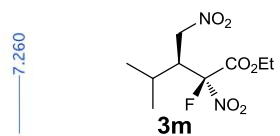
Minor diastereomer (31')





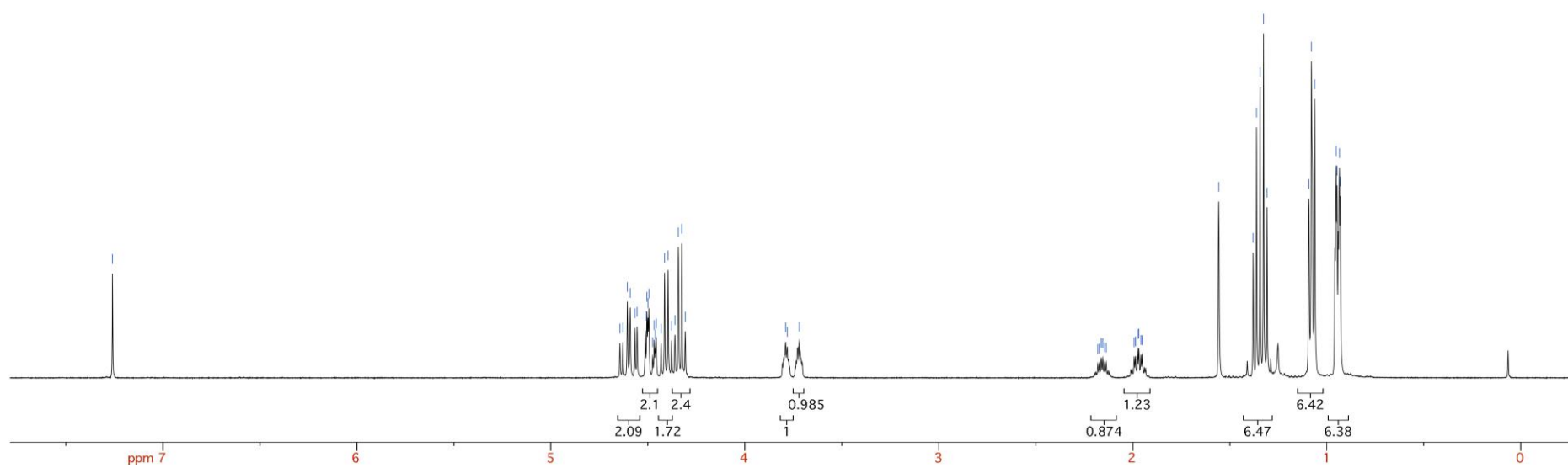


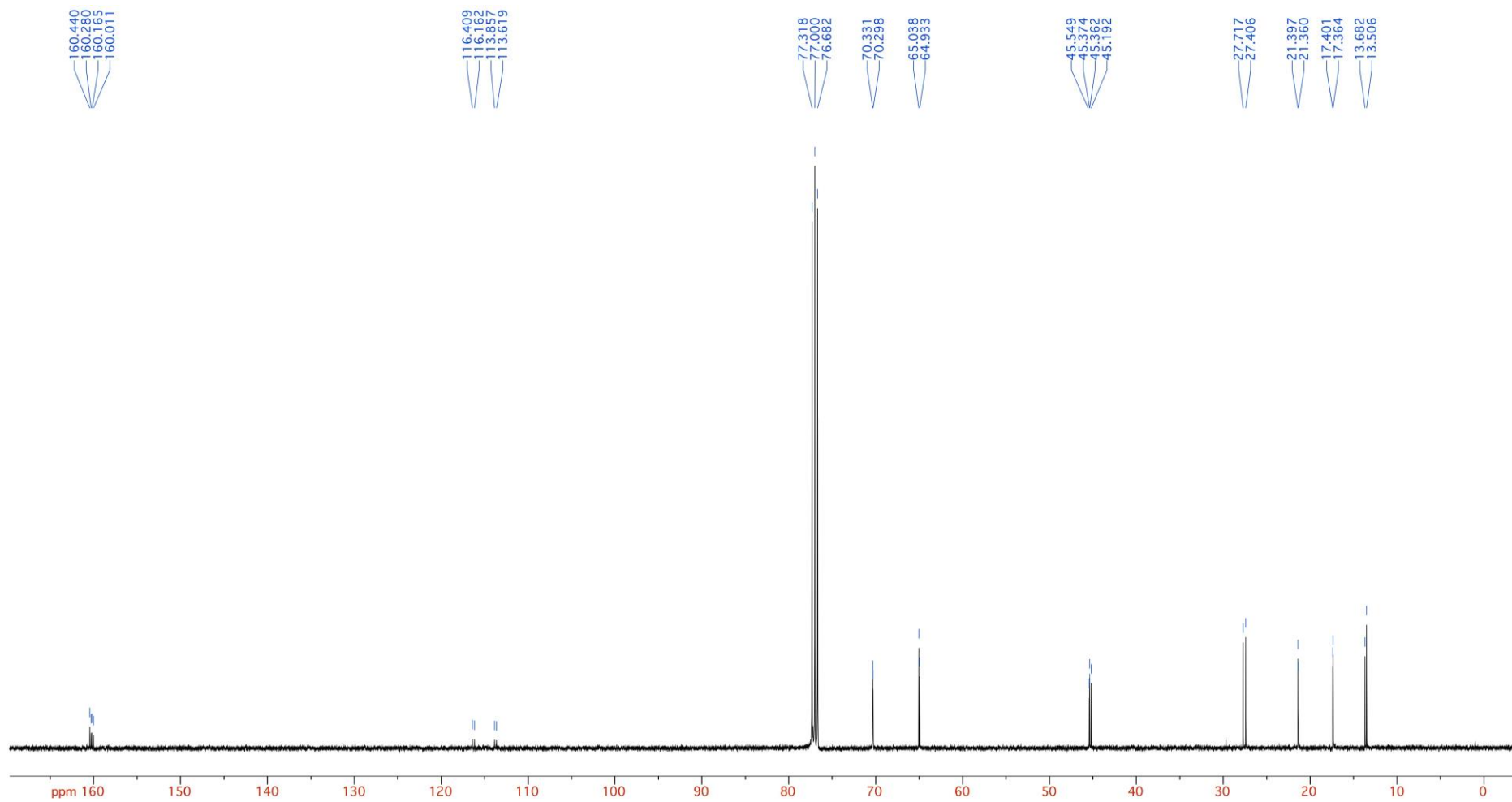
Diastereomeric mixture (3m)

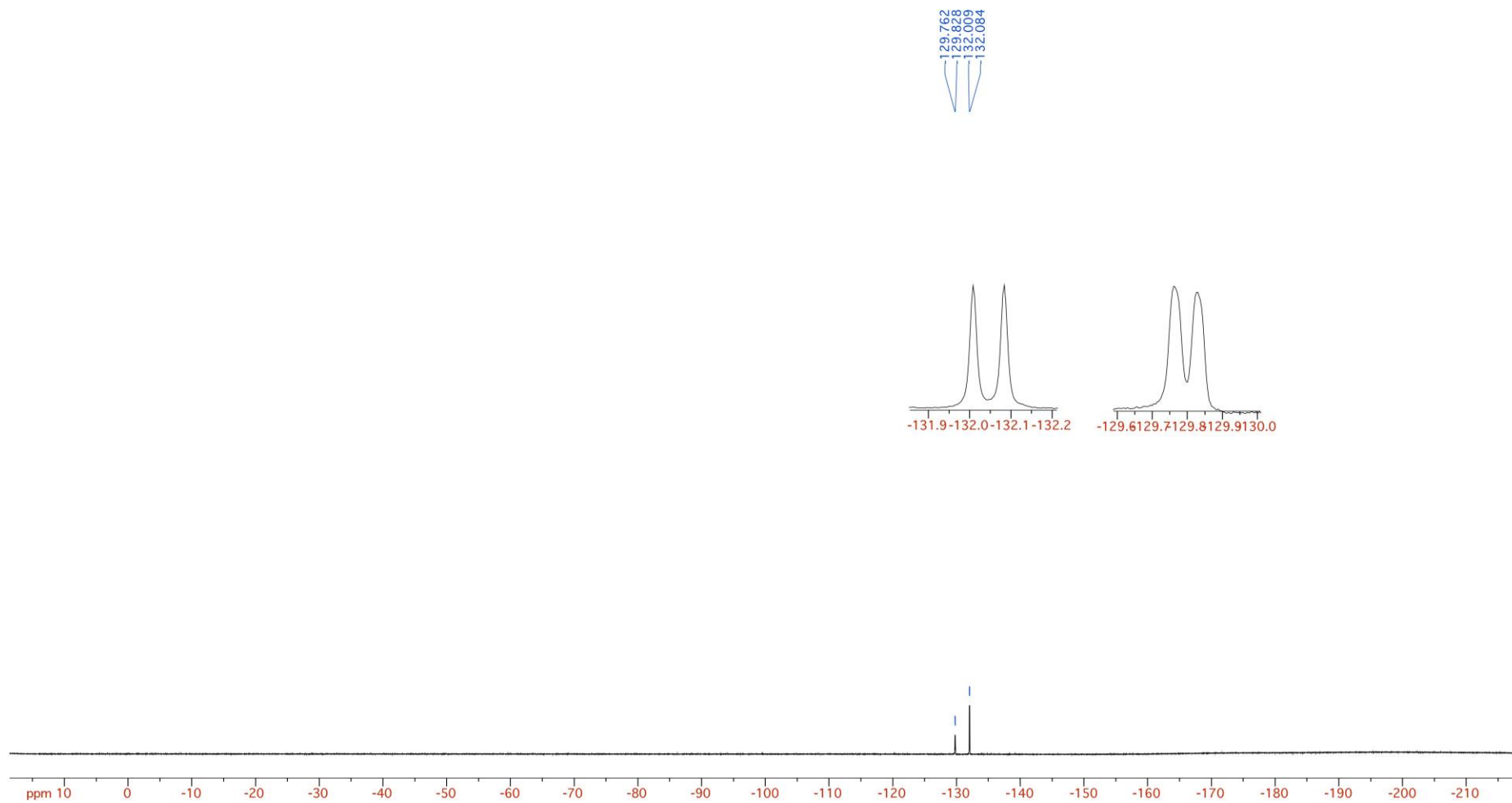


4.644
4.639
4.606
4.591
4.567
4.556
4.513
4.505
4.495
4.472
4.462
4.452
4.414
4.396
4.378
4.361
4.343
4.325
4.290
4.280
4.219

2.180
2.172
2.155
2.145
2.137
1.986
1.975
1.969
1.958
1.951
1.557
1.380
1.362
1.344
1.326
1.079
1.062
0.952
0.948
0.935
0.931

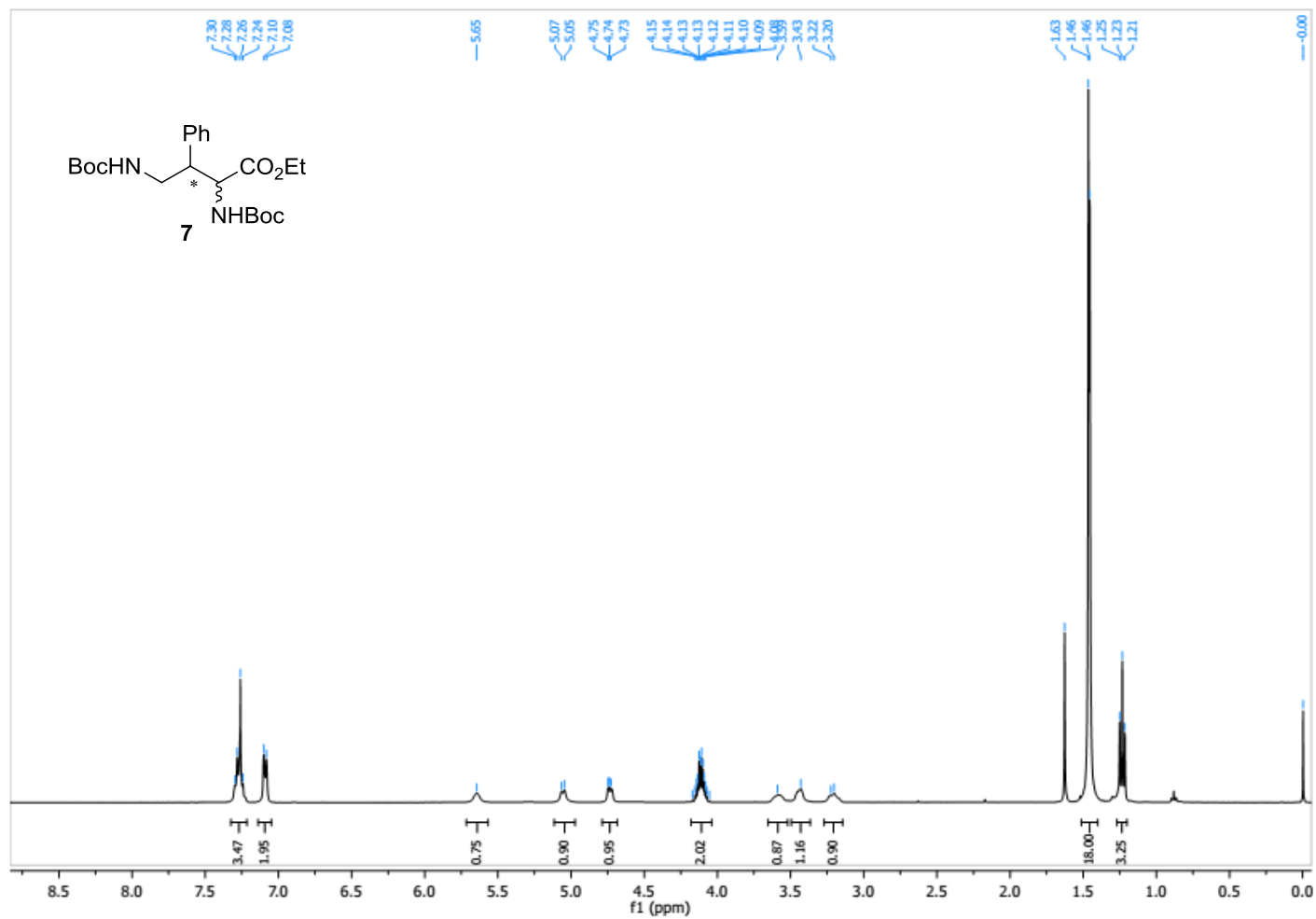


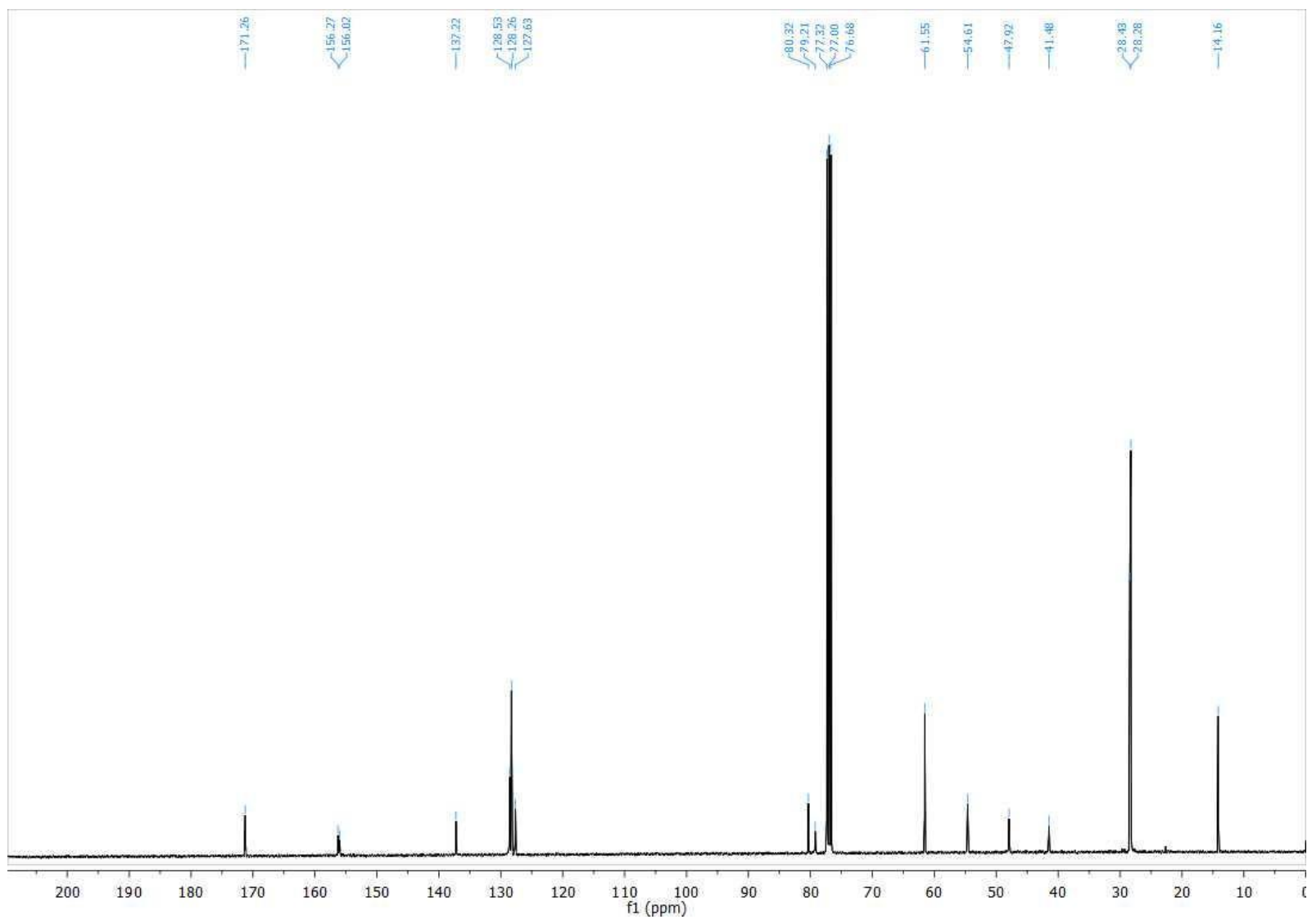




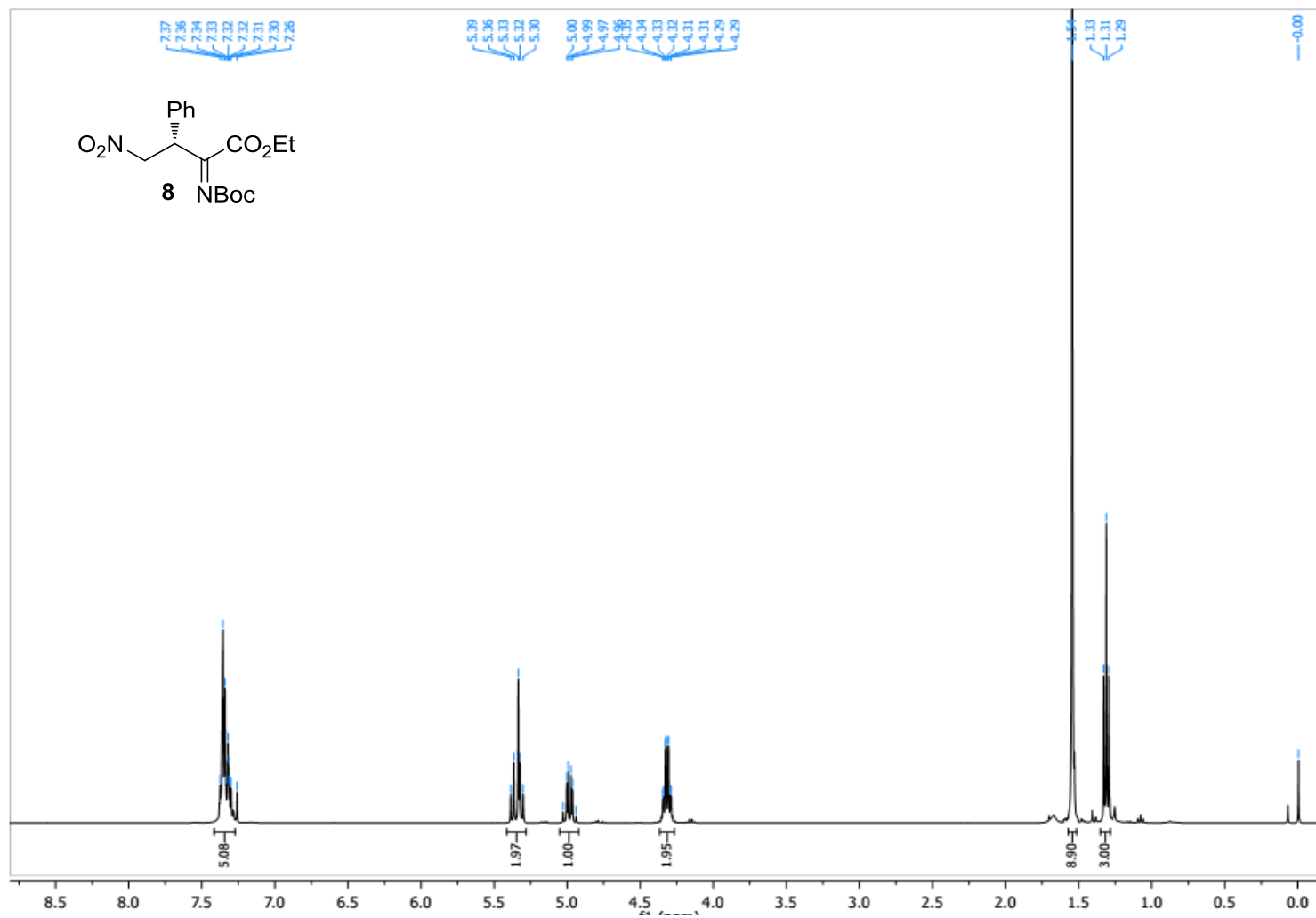
E. NMR Spectra of the Derivatives and Mannich Addition Product

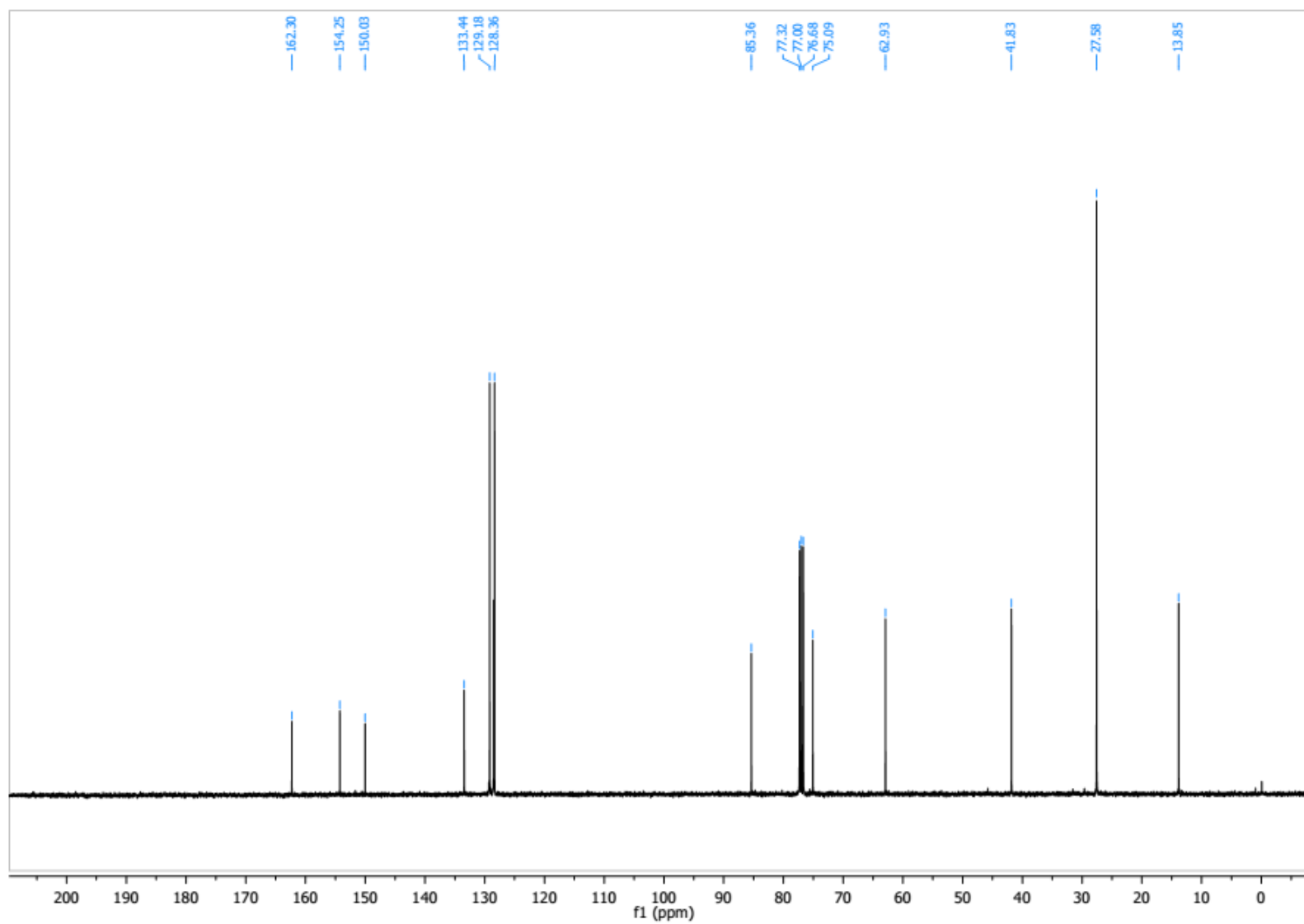
Ethyl 2,4-bis((tert-butoxycarbonyl)amino)-3-phenylbutanoate (7)



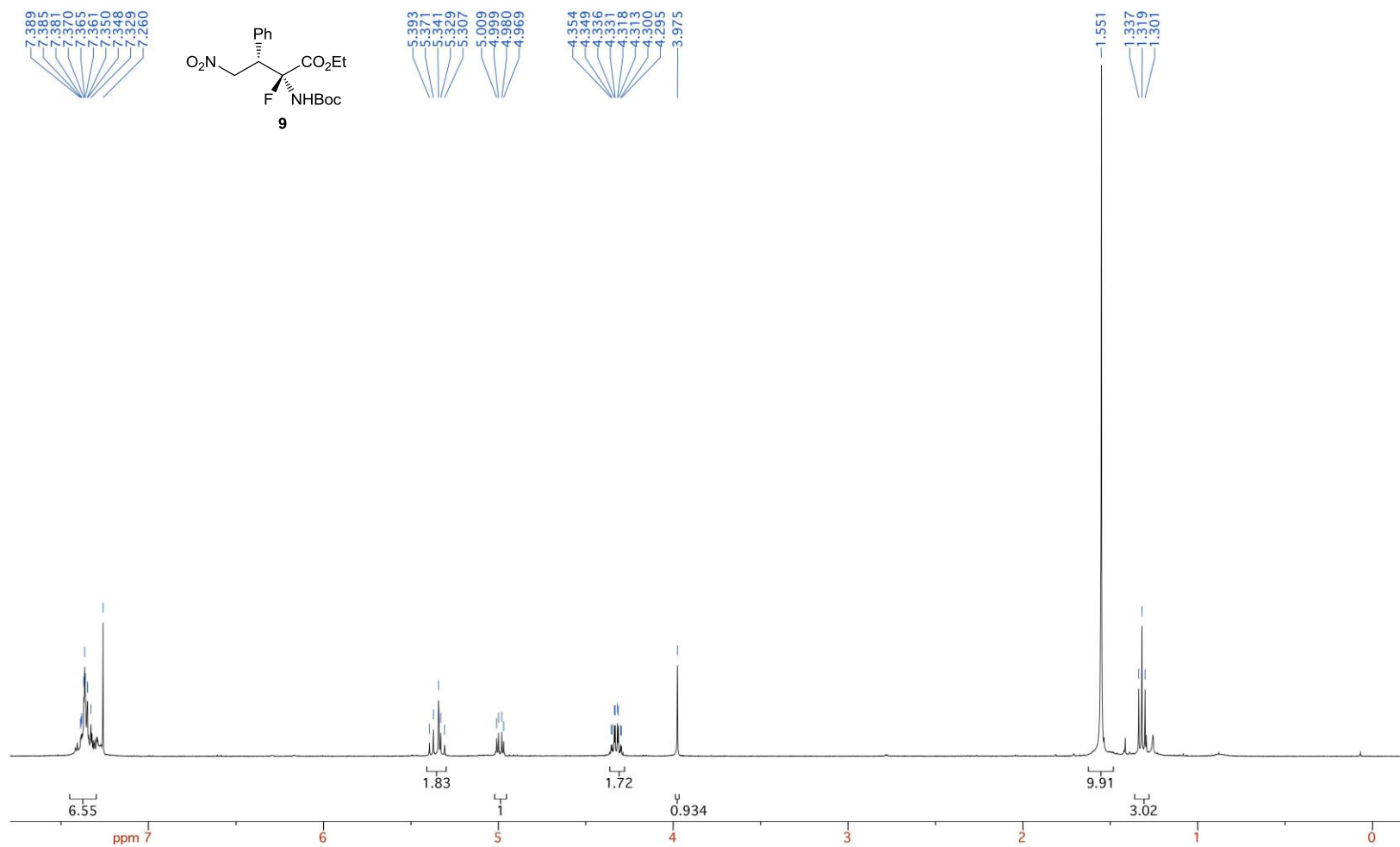


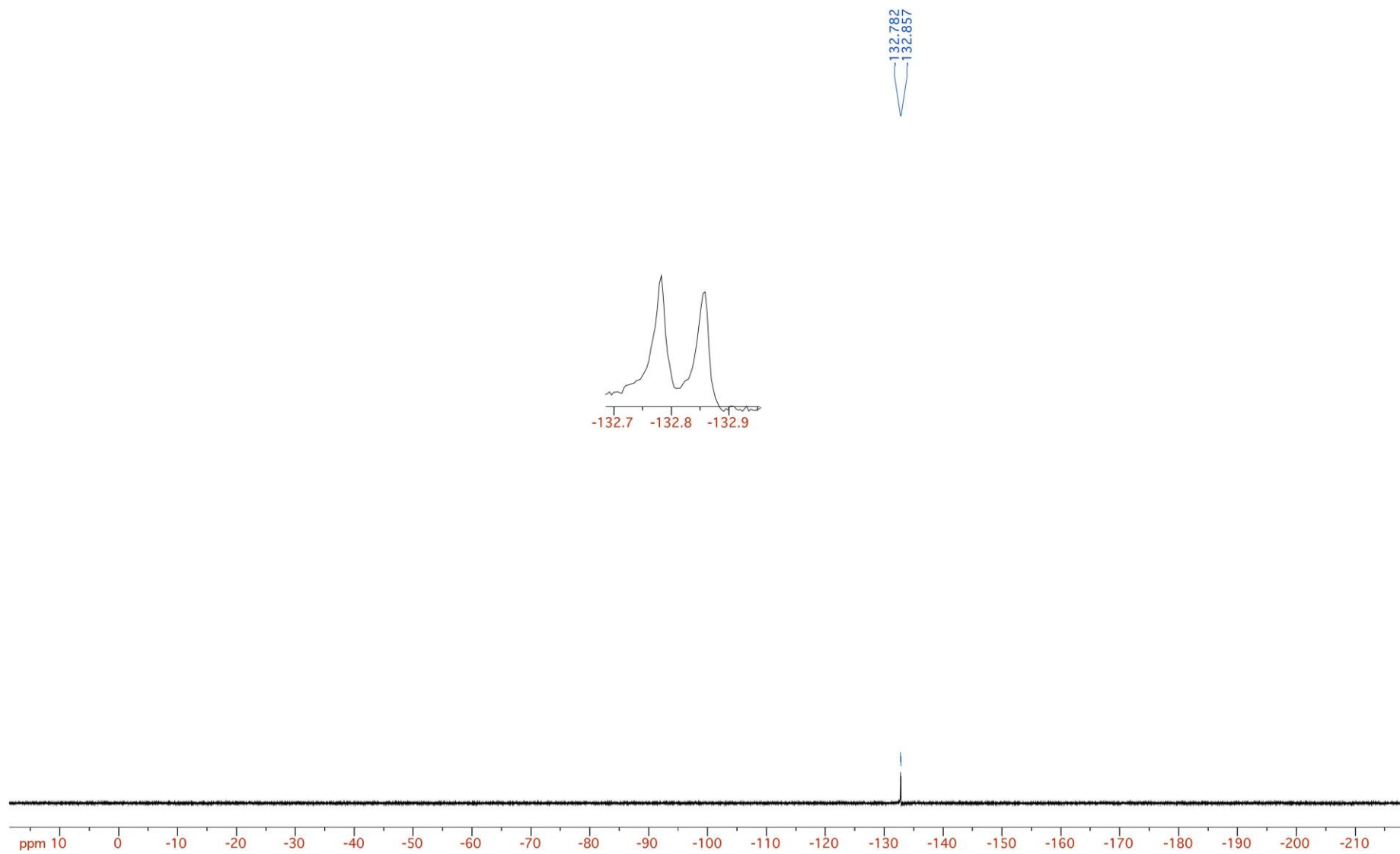
(S)-Ethyl 2-((tert-butoxycarbonyl)imino)-4-nitro-3-phenylbutanoate (**8**)

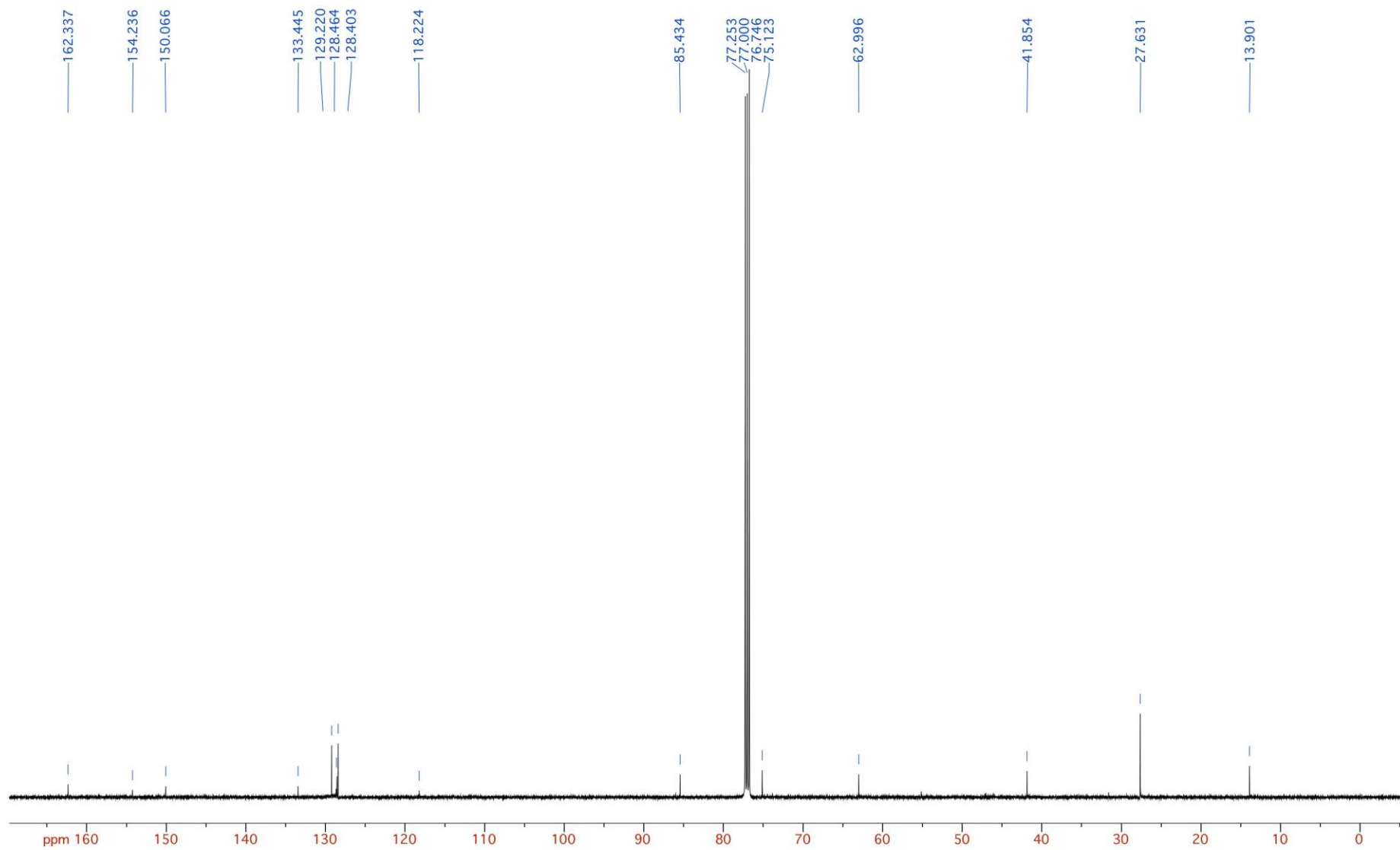




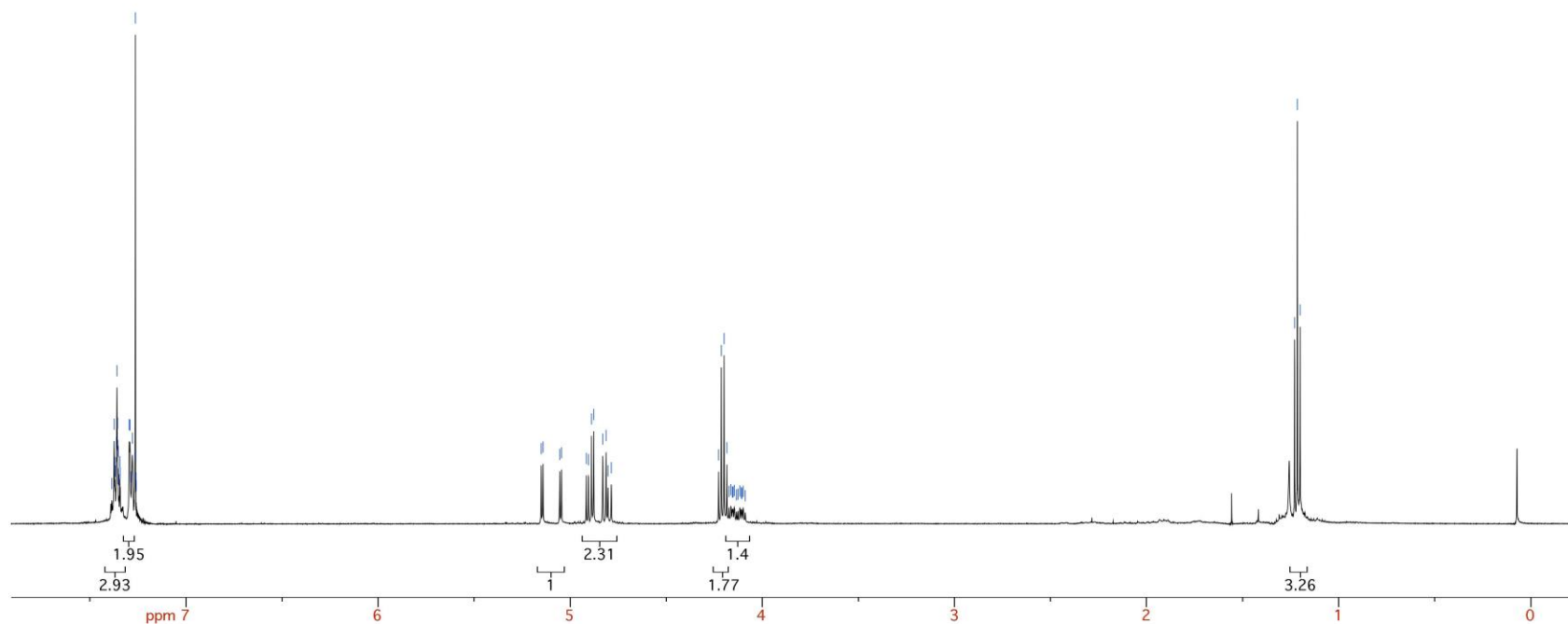
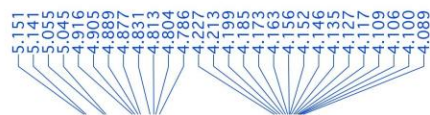
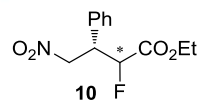
(2S,3S)-Ethyl 2-((tert-butoxycarbonyl)amino)-2-fluoro-4-nitro-3-phenylbutanoate (9)

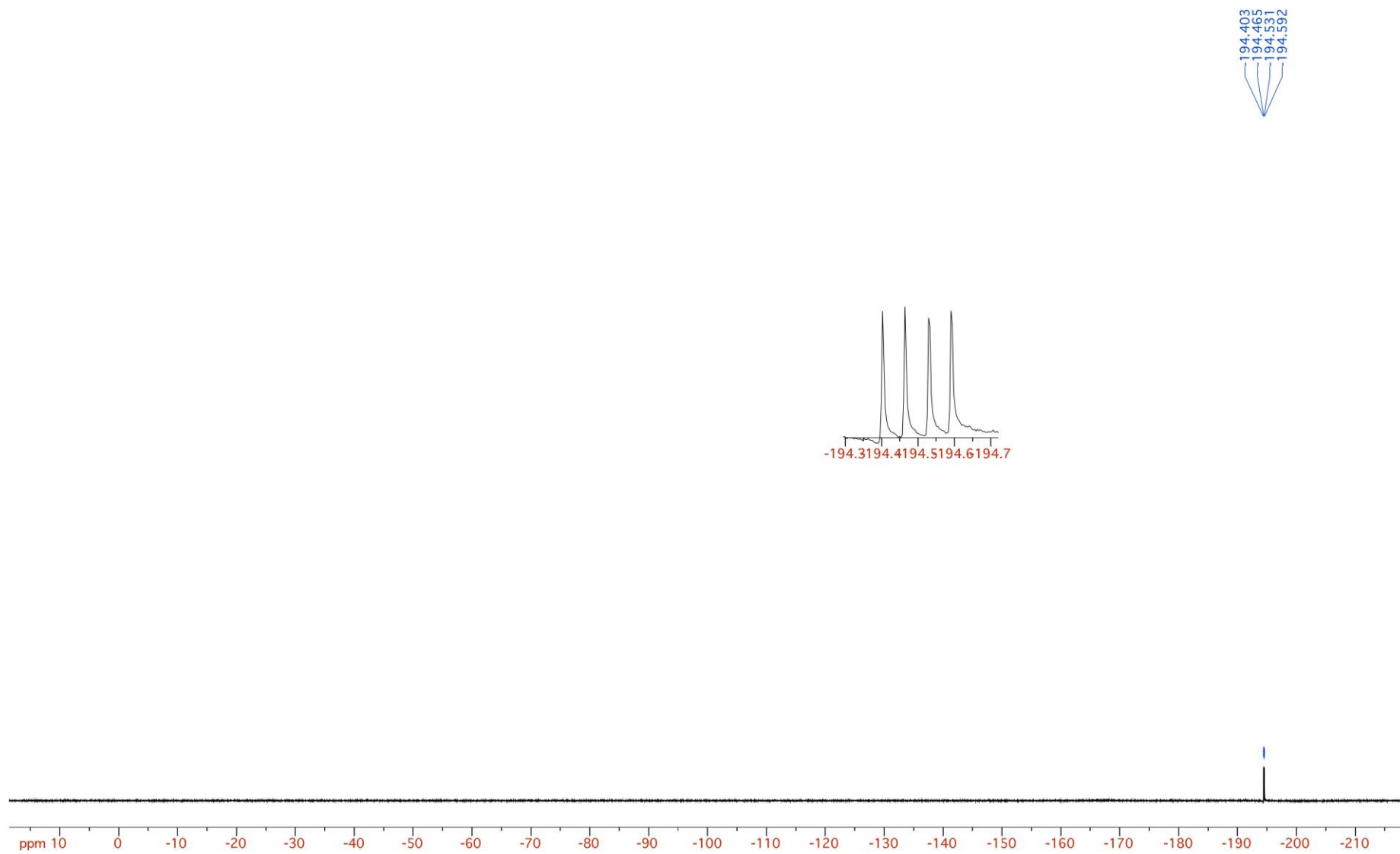


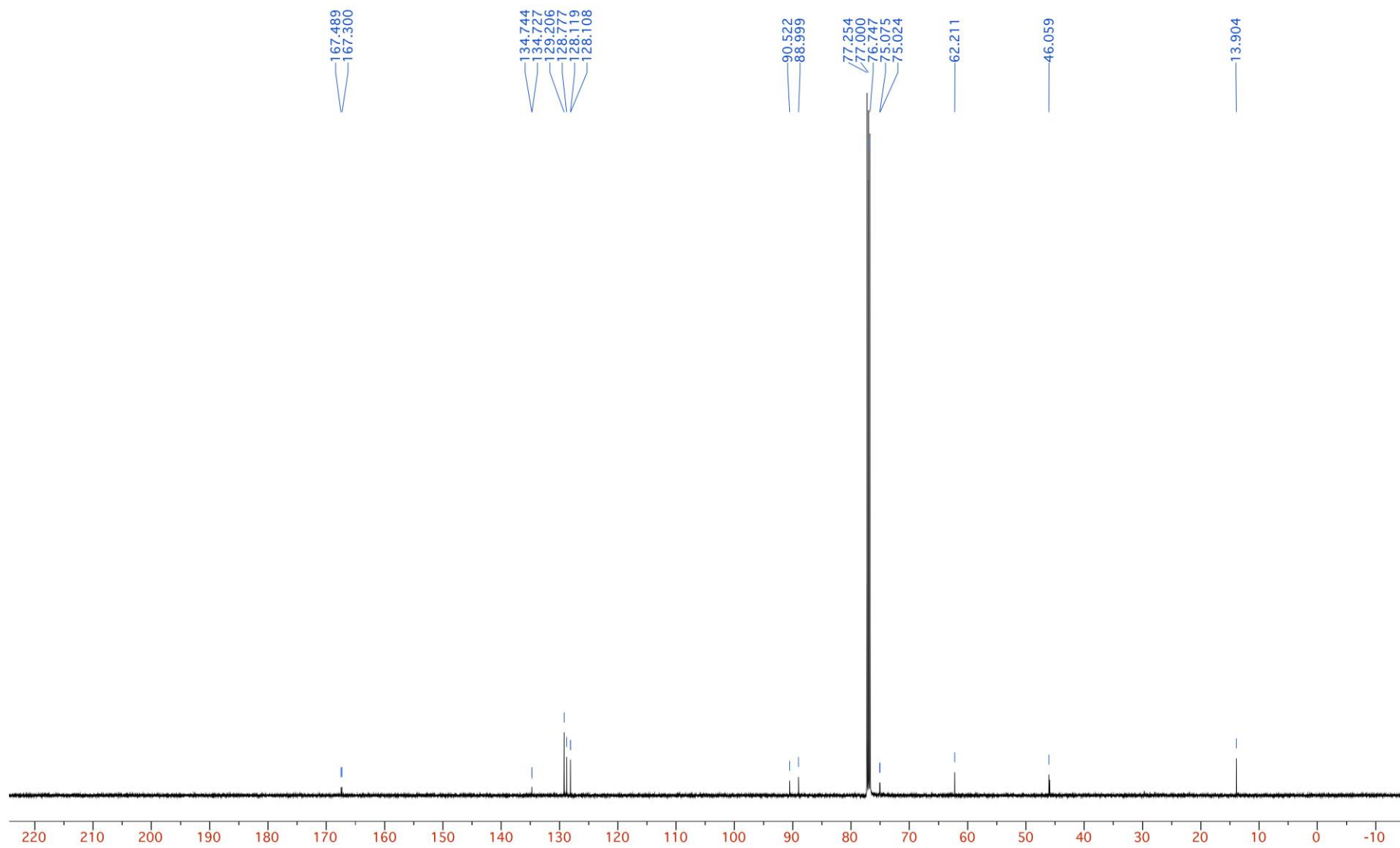




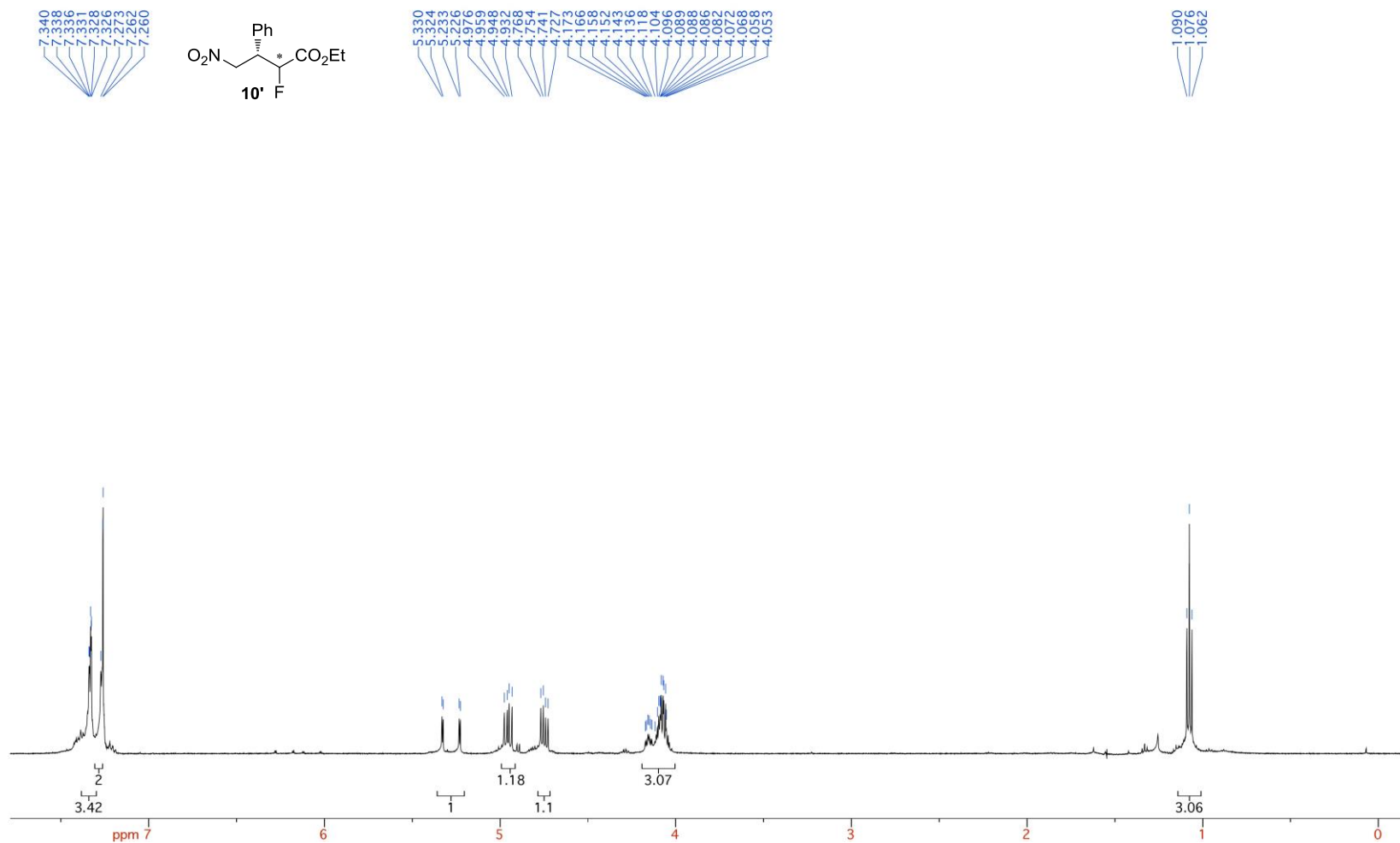
((2S)-1-fluoro-1,3-dinitropropan-2-yl)benzene (10, pure major diastereomer)

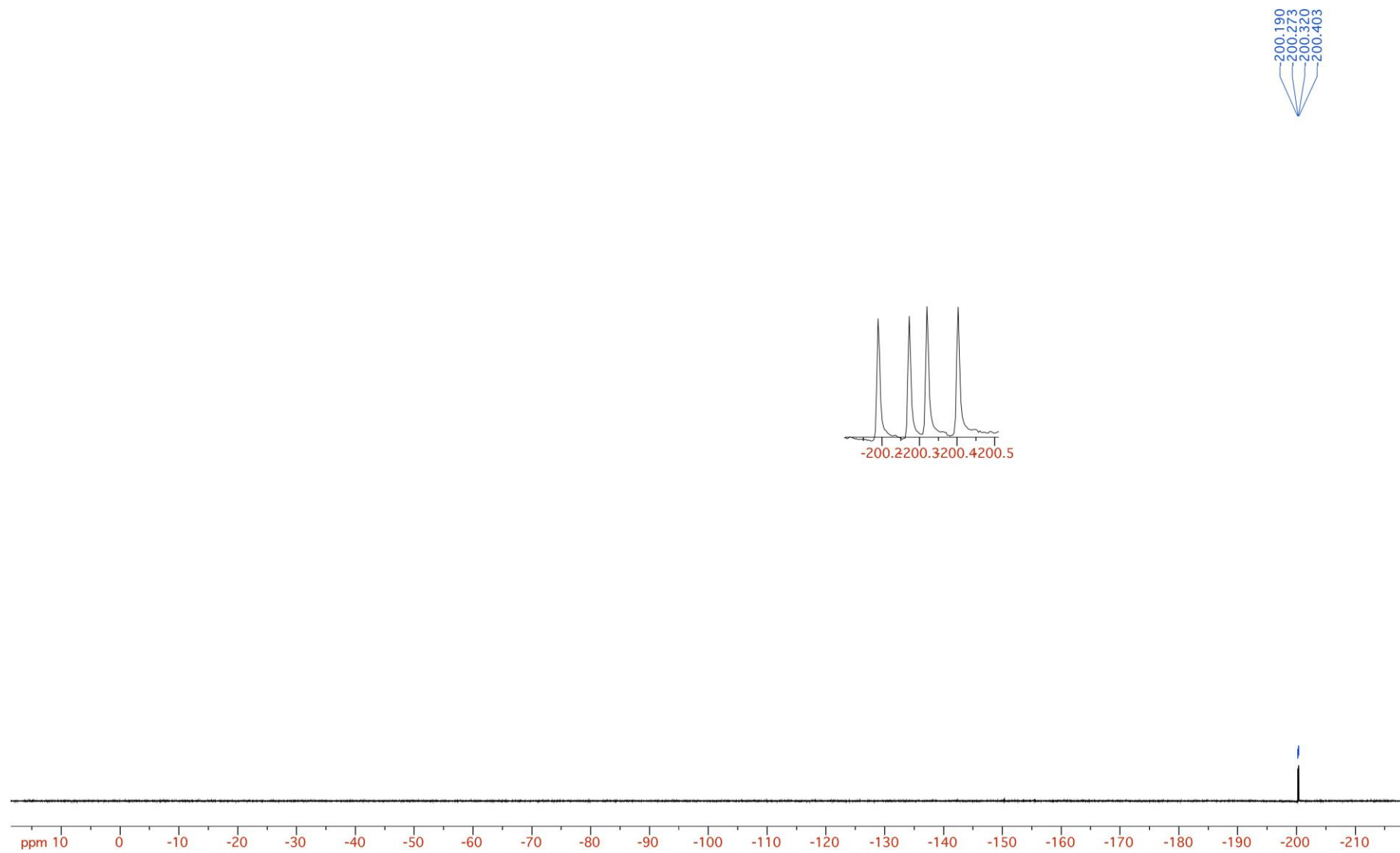


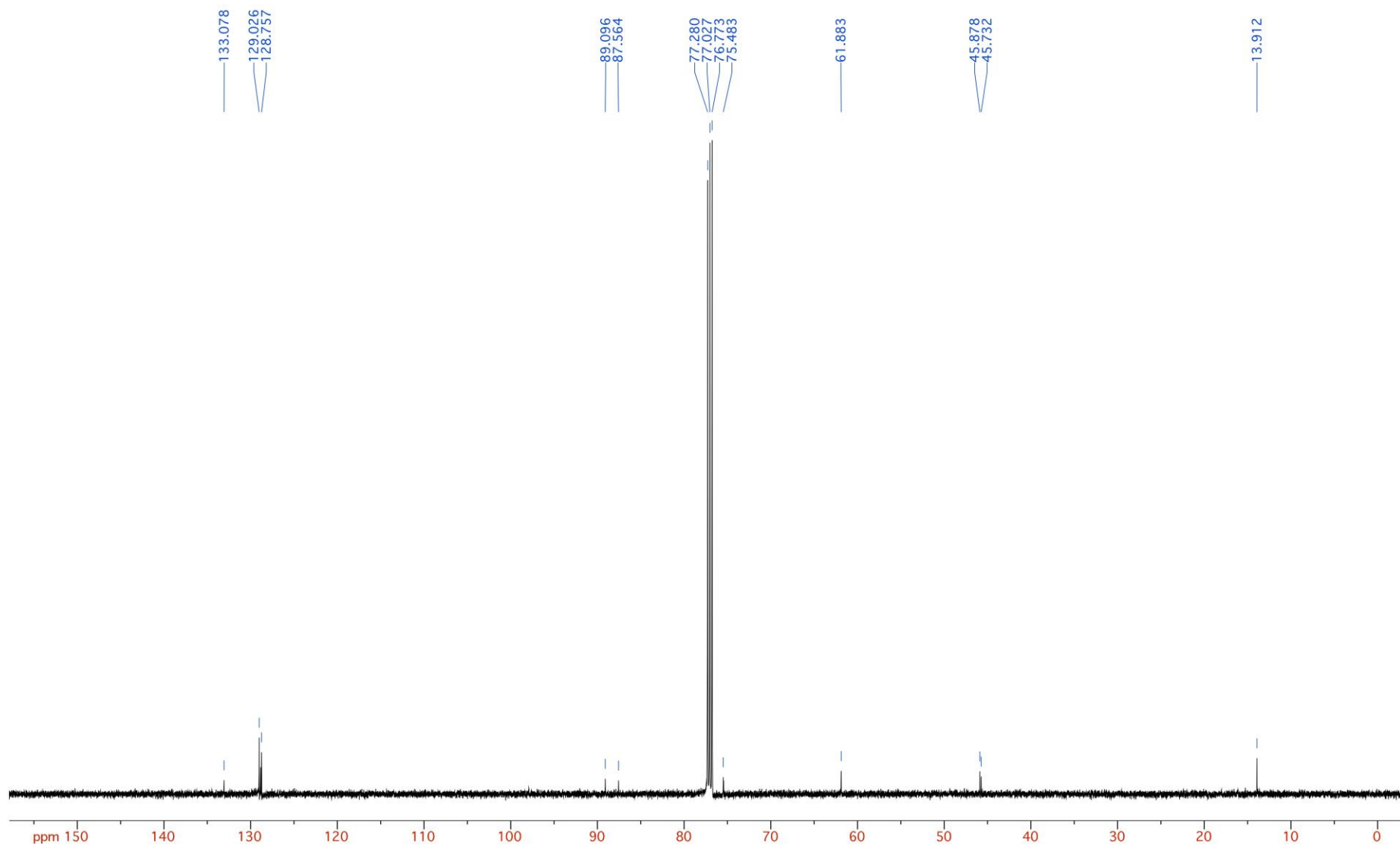




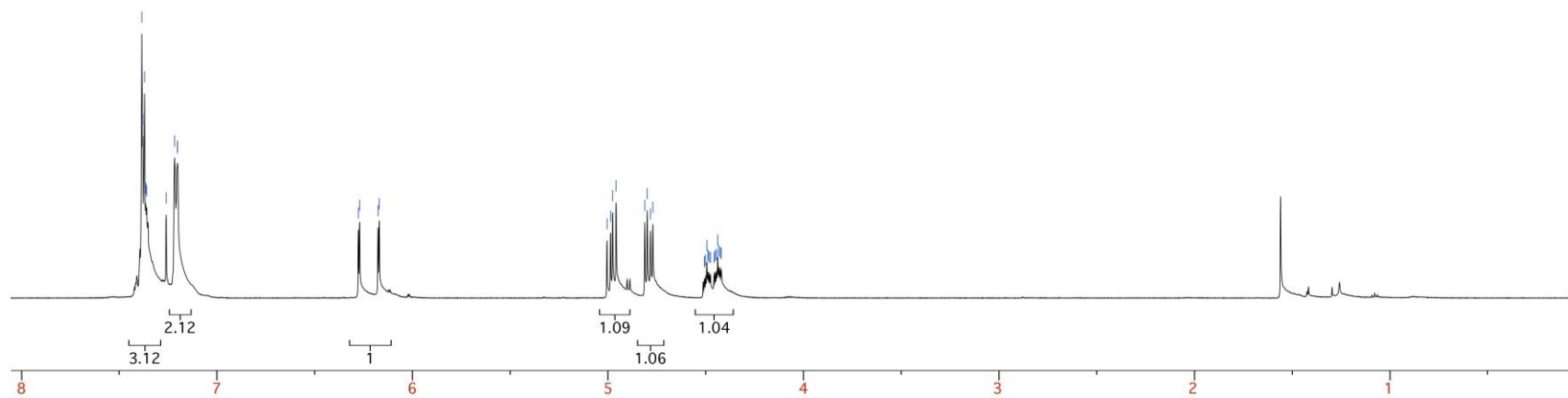
((2S)-1-fluoro-1,3-dinitropropan-2-yl)benzene (10', pure minor diastereomer)

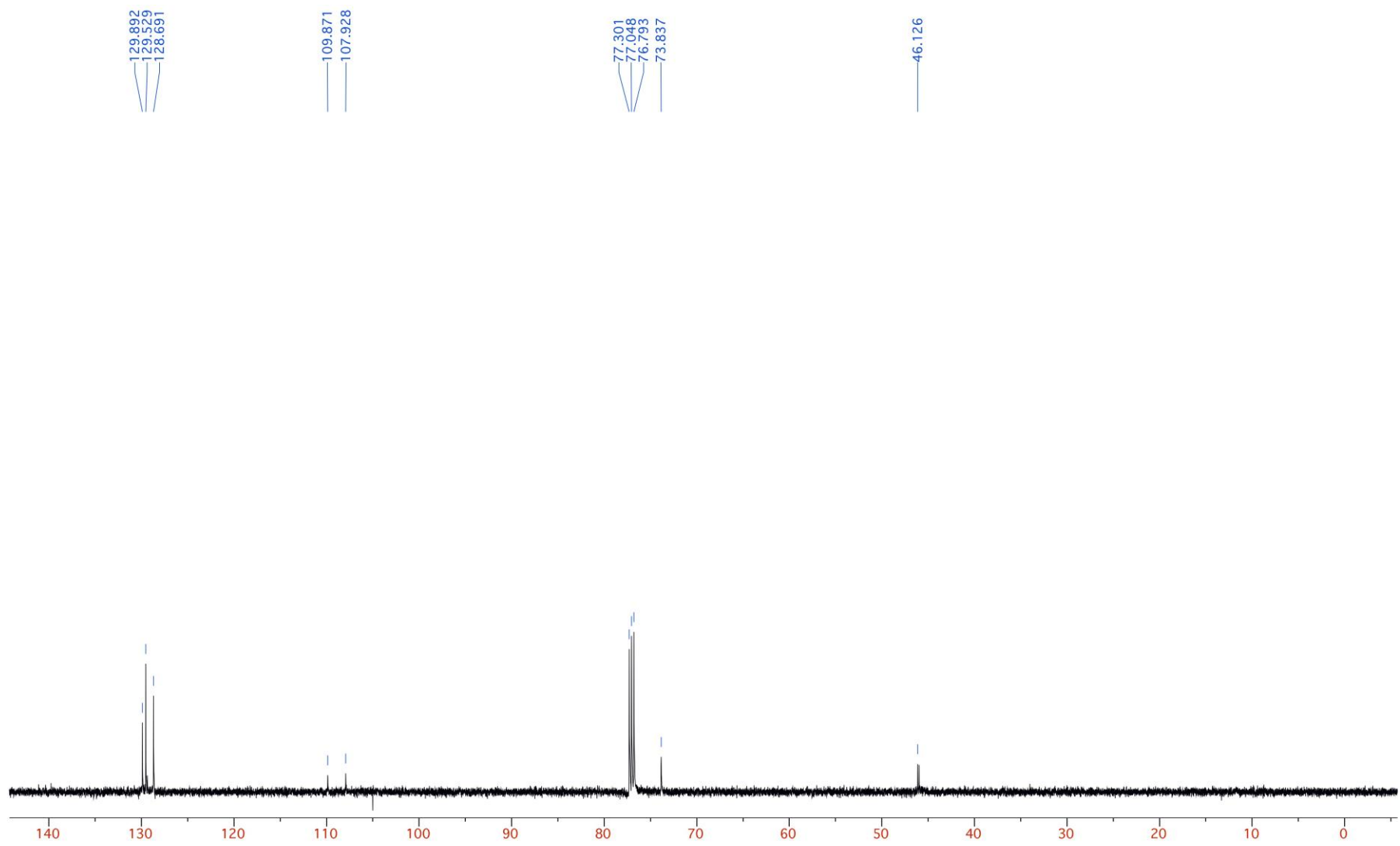


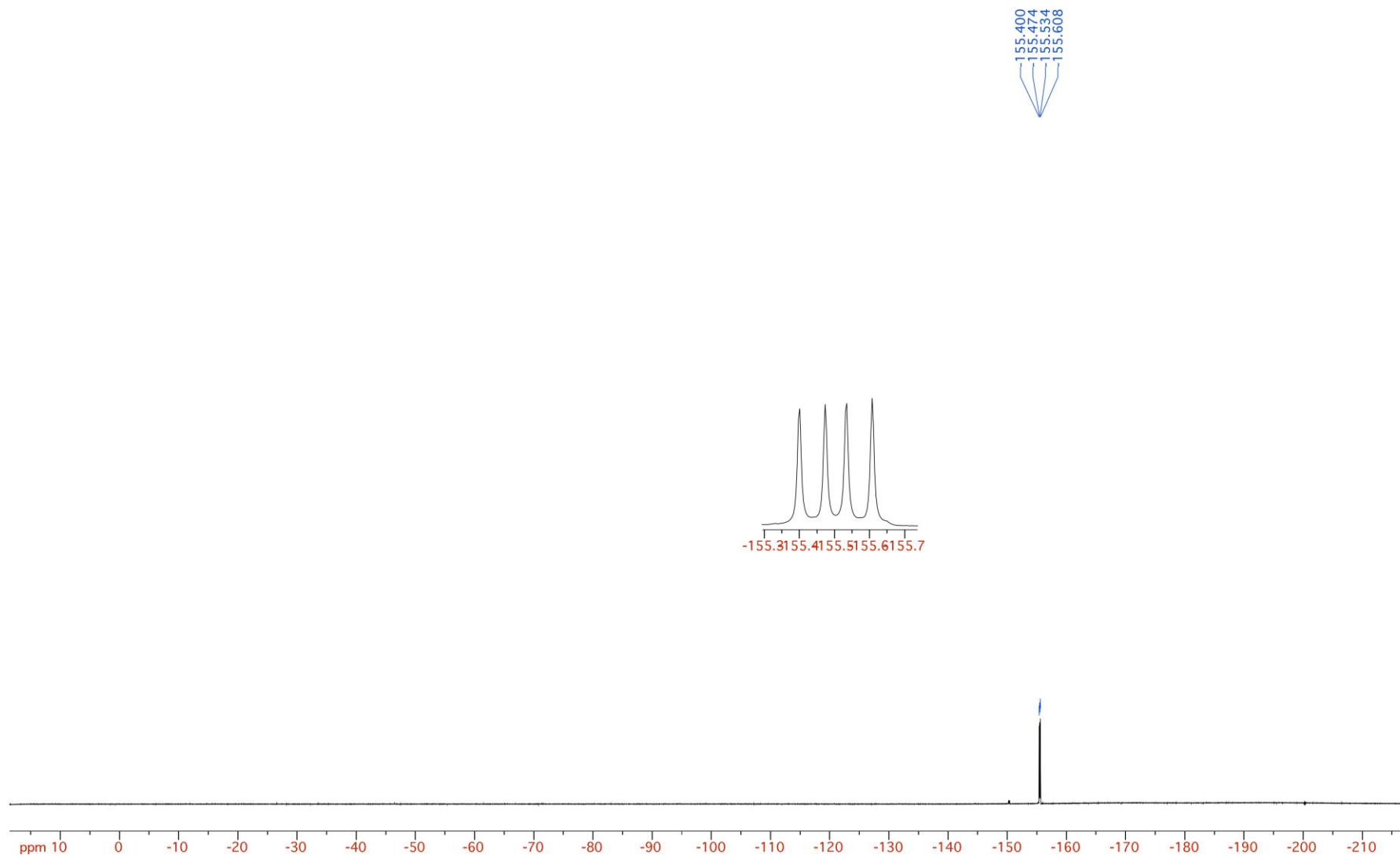




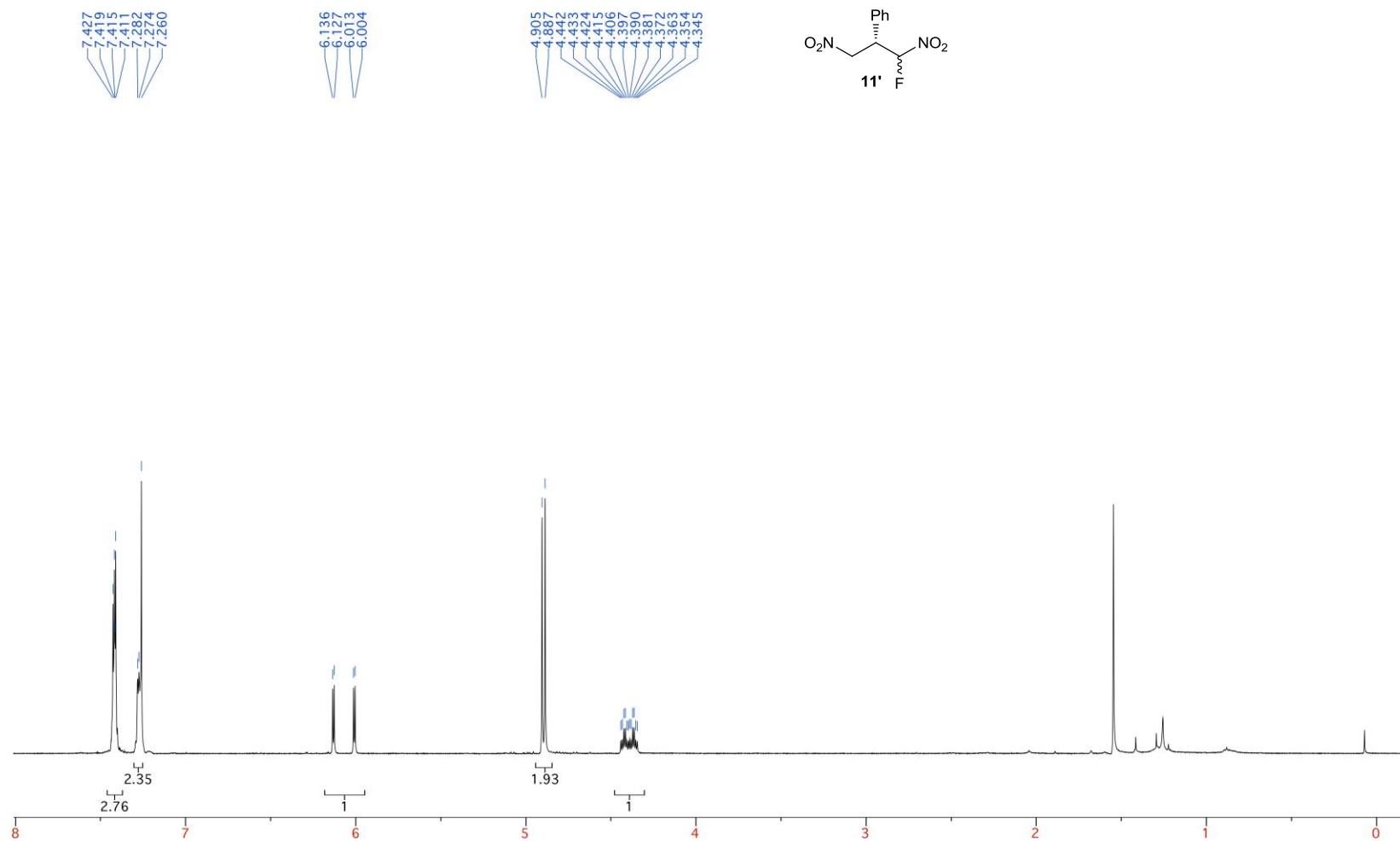
((2S)-1-Fluoro-1,3-dinitropropan-2-yl)benzene (11, pure major diastereomer)

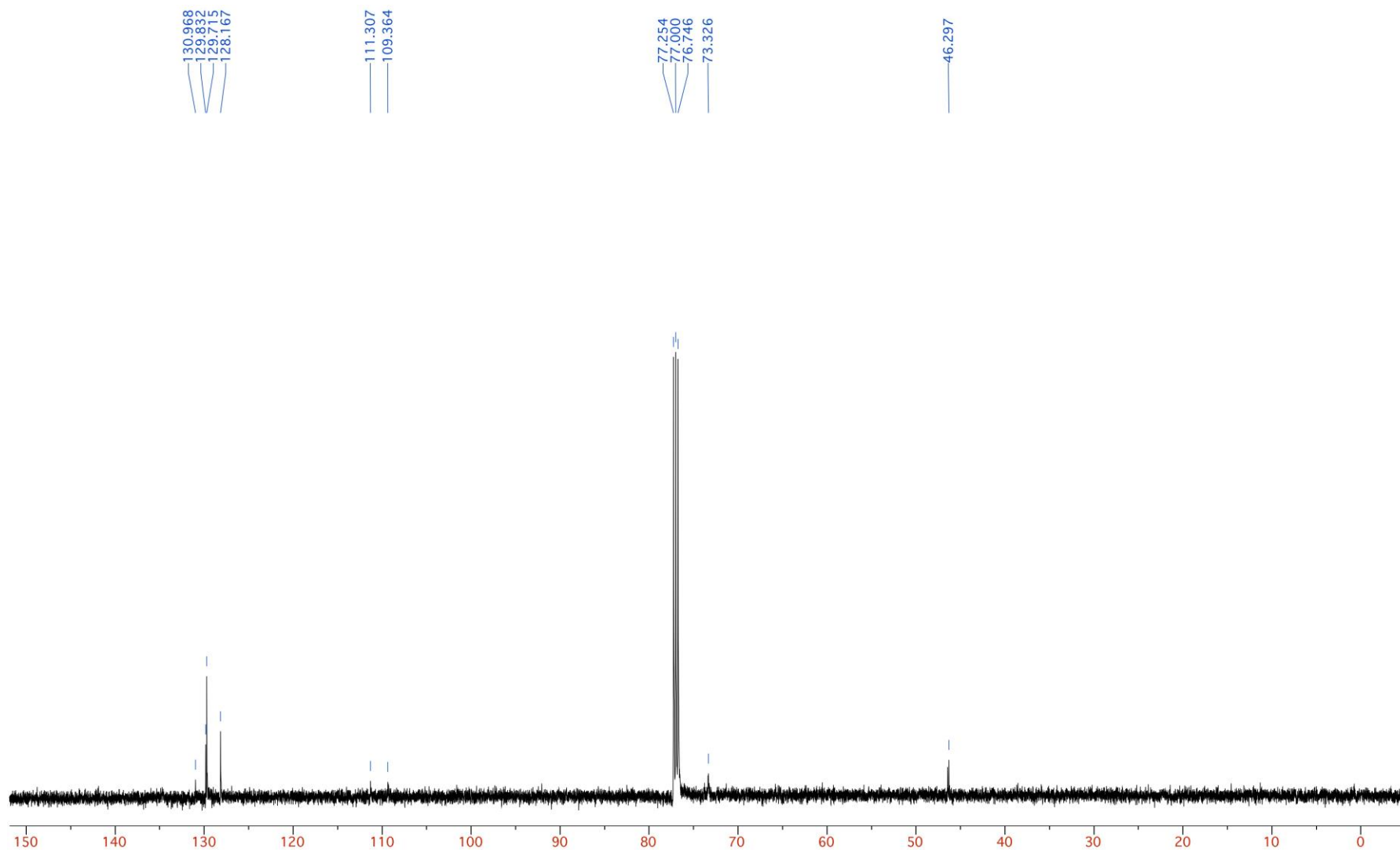


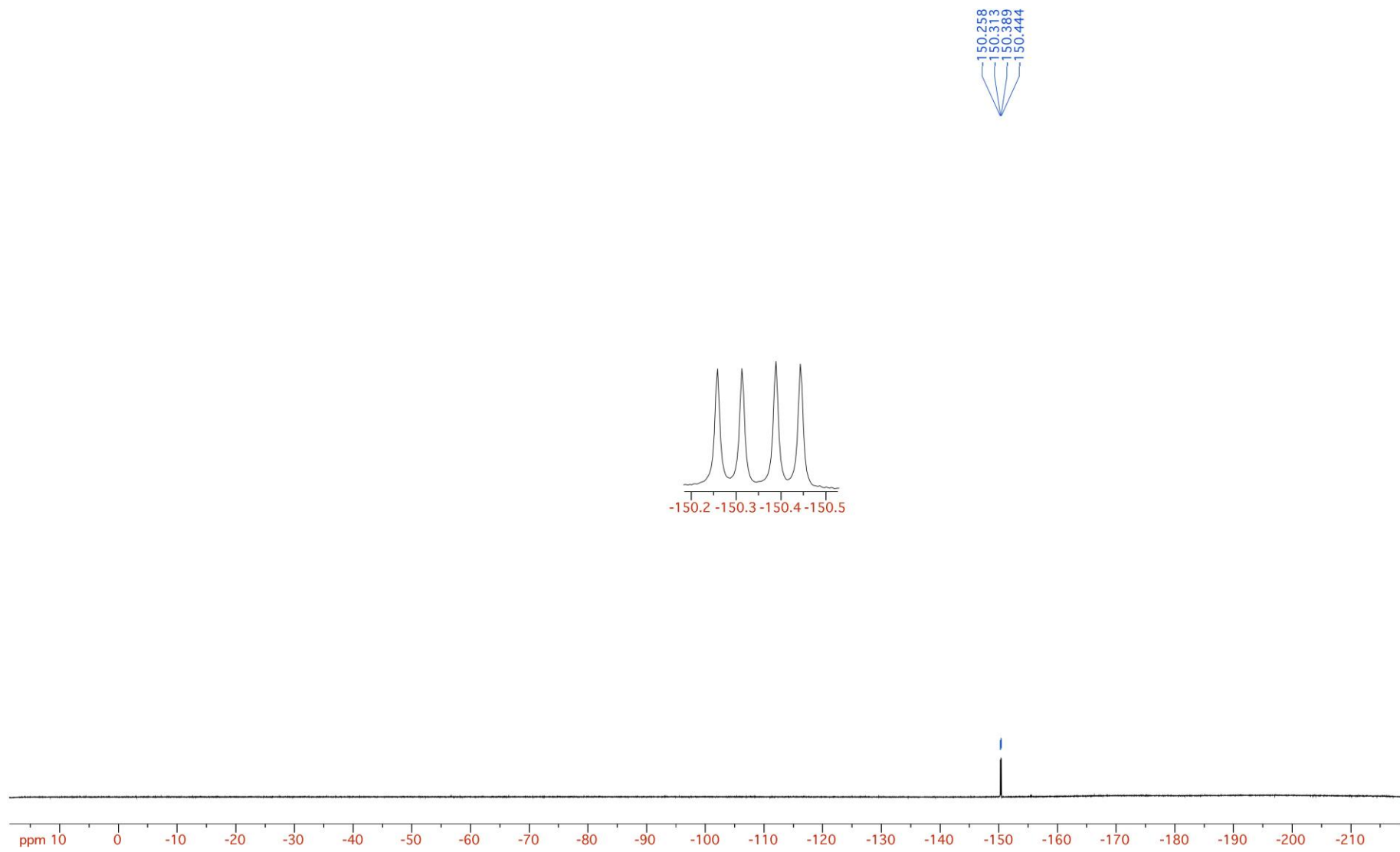




((2S)-1-Fluoro-1,3-dinitropropan-2-yl)benzene (11', pure minor diastereomer)







Ethyl 3-((tert-butoxycarbonyl)amino)-2-fluoro-2-nitro-3-phenylpropanoate (13, diastereomeric mixture)

