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Synthesis and Structural Features of α -Fluorocarbonyl Systems

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Sustainable synthesis of enantiopure fluorolactam derivatives by a selective direct fluorination - amidase strategy

Nicky J. Willis,^a Craig A. Fisher,^b Catherine M. Alder,^a Antal Harsanyi,^b Lena Shukla^{*a} Joseph P. Adams,^a and Graham Sandford^{*b}

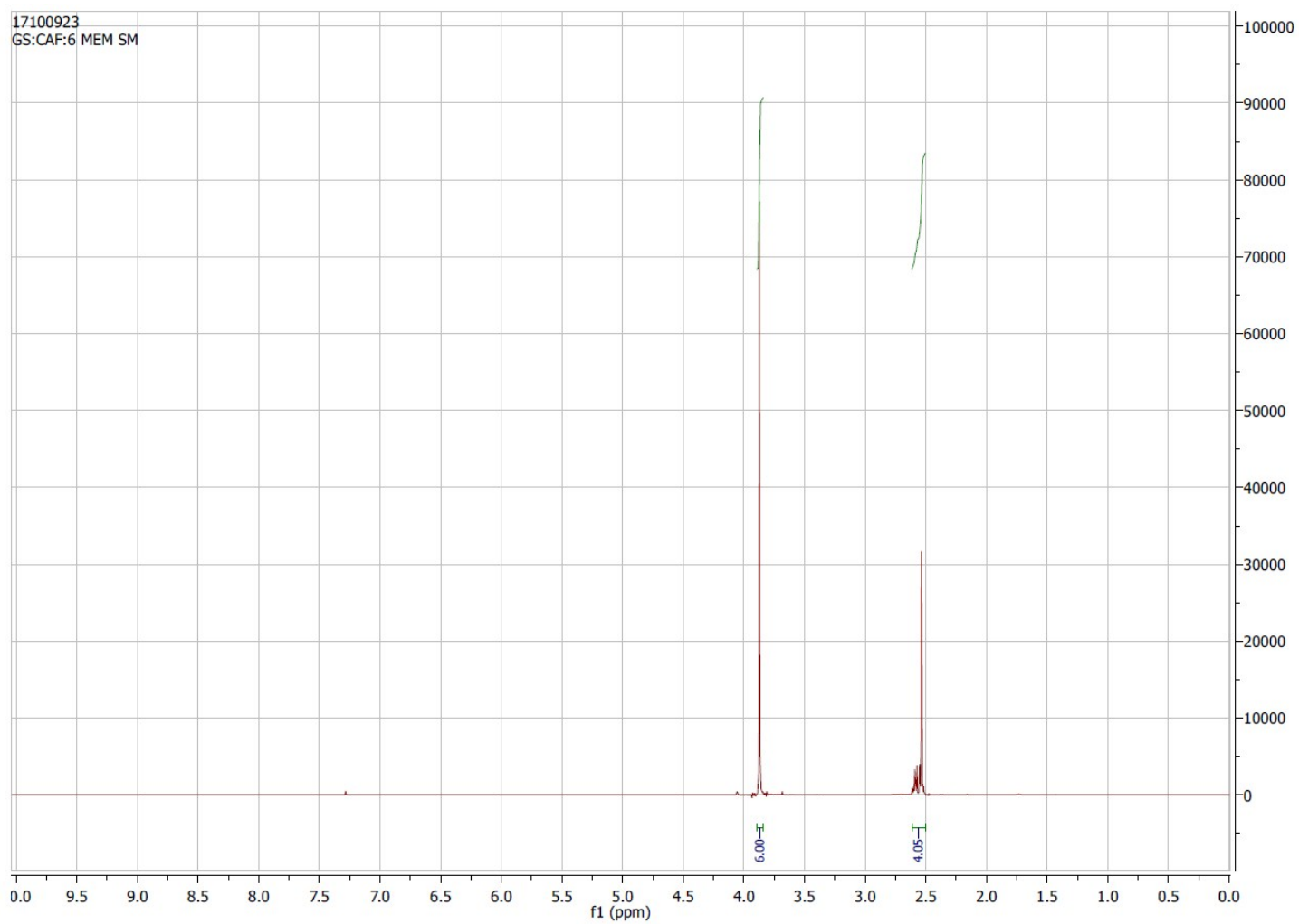
SUPPORTING INFORMATION 5

NMR Spectra

SI-5.1	Dimethyl 2-(2-cyanoethyl)-2-fluoromalonate 4b	2
SI-5.2	Dimethyl 2-(3-aminopropyl)-2-fluoromalonate, hydrochloride salt 4c	5
SI-5.3	Methyl 3-fluoro-2-oxo-3-piperidine carboxylate 4d	8
SI-5.4	3-Fluoro-2-oxopiperidine-3-carboxylic acid 5	11
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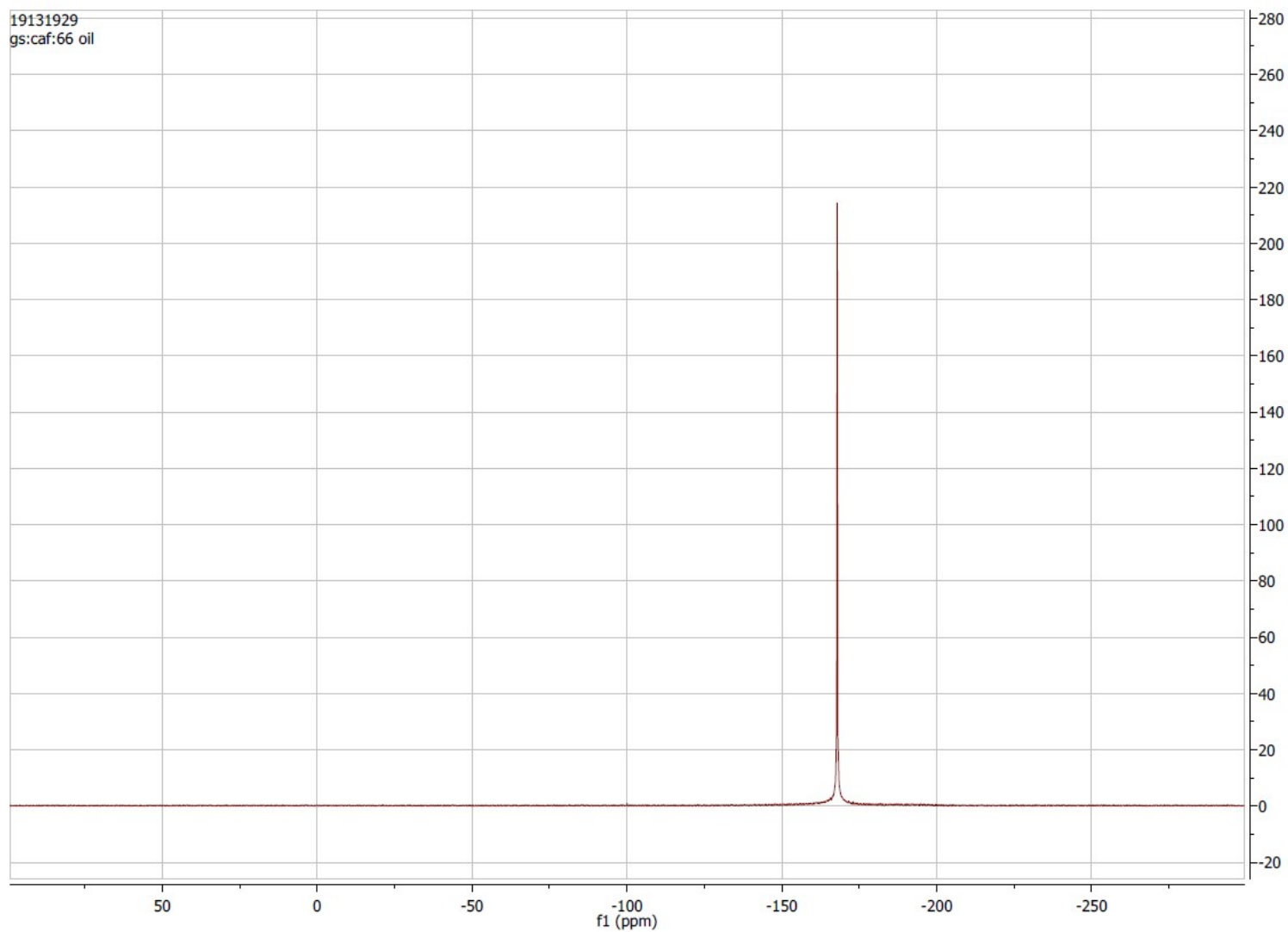
SI-5.1 Dimethyl 2-(2-cyanoethyl)-2-fluoromalonate **4b**

^1H NMR spectrum



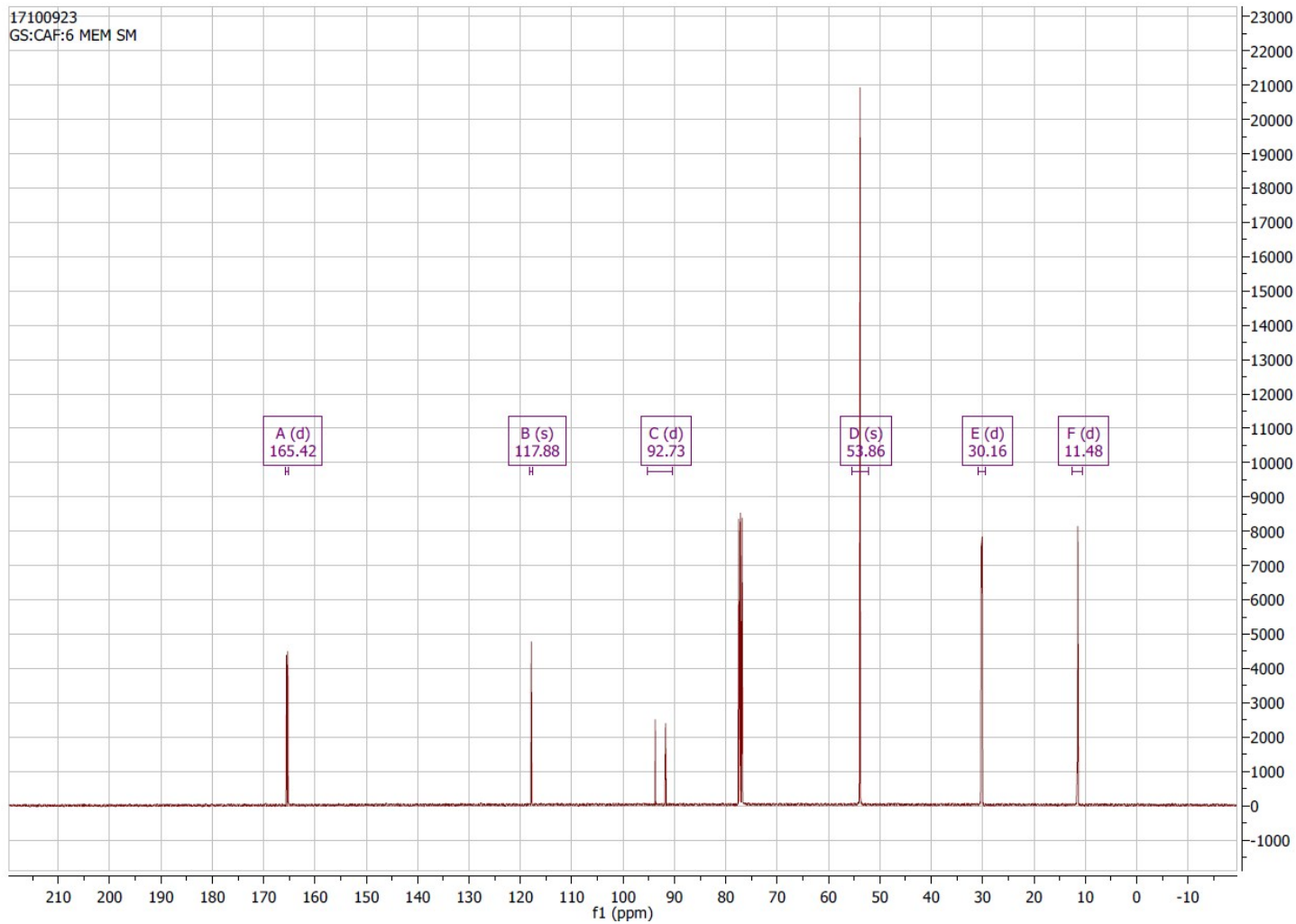
Dimethyl 2-(2-cyanoethyl)-2-fluoromalonate **4b**

^{19}F NMR spectrum



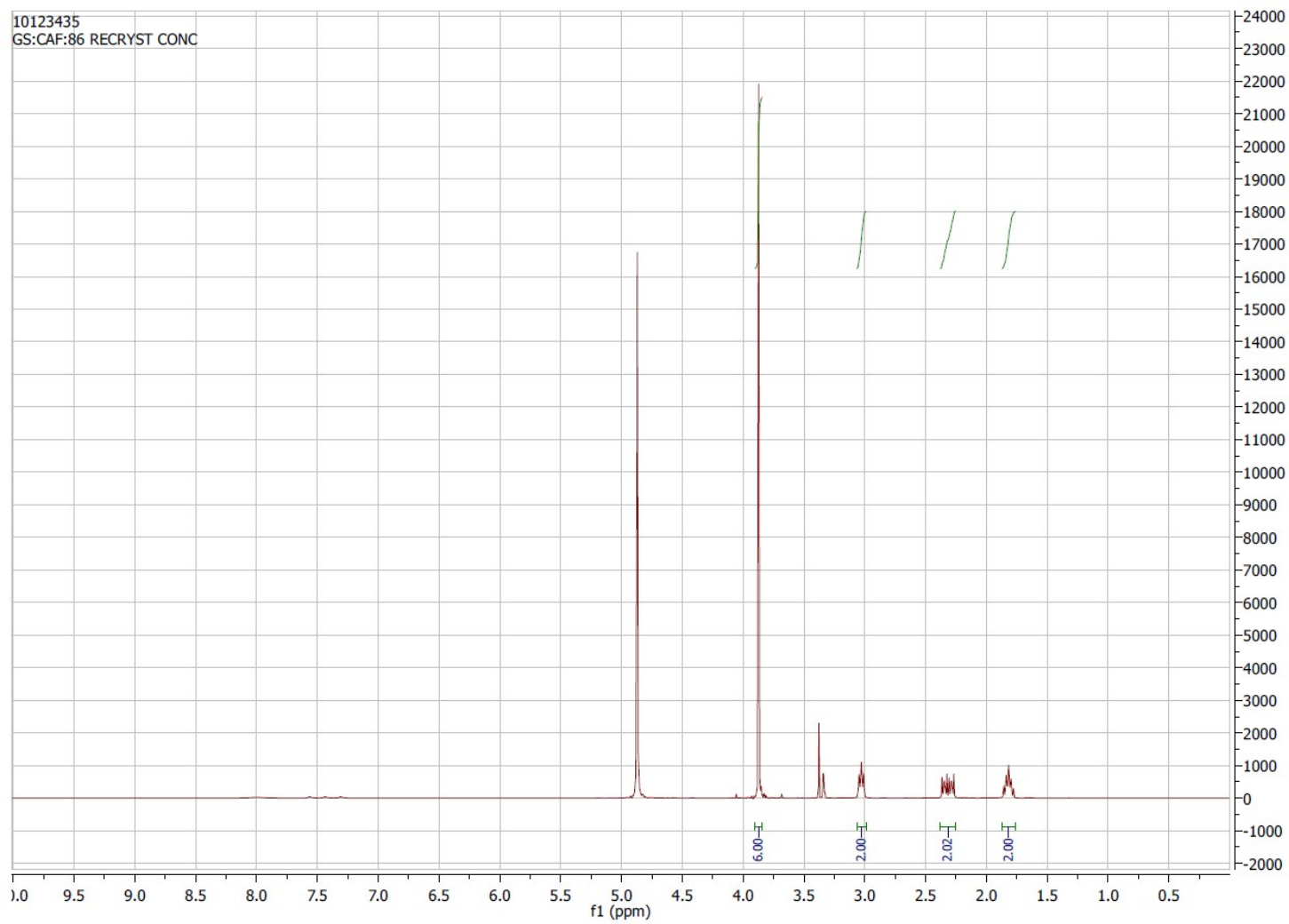
Dimethyl 2-(2-cyanoethyl)-2-fluoromalonate **4b**

^{13}C NMR spectrum



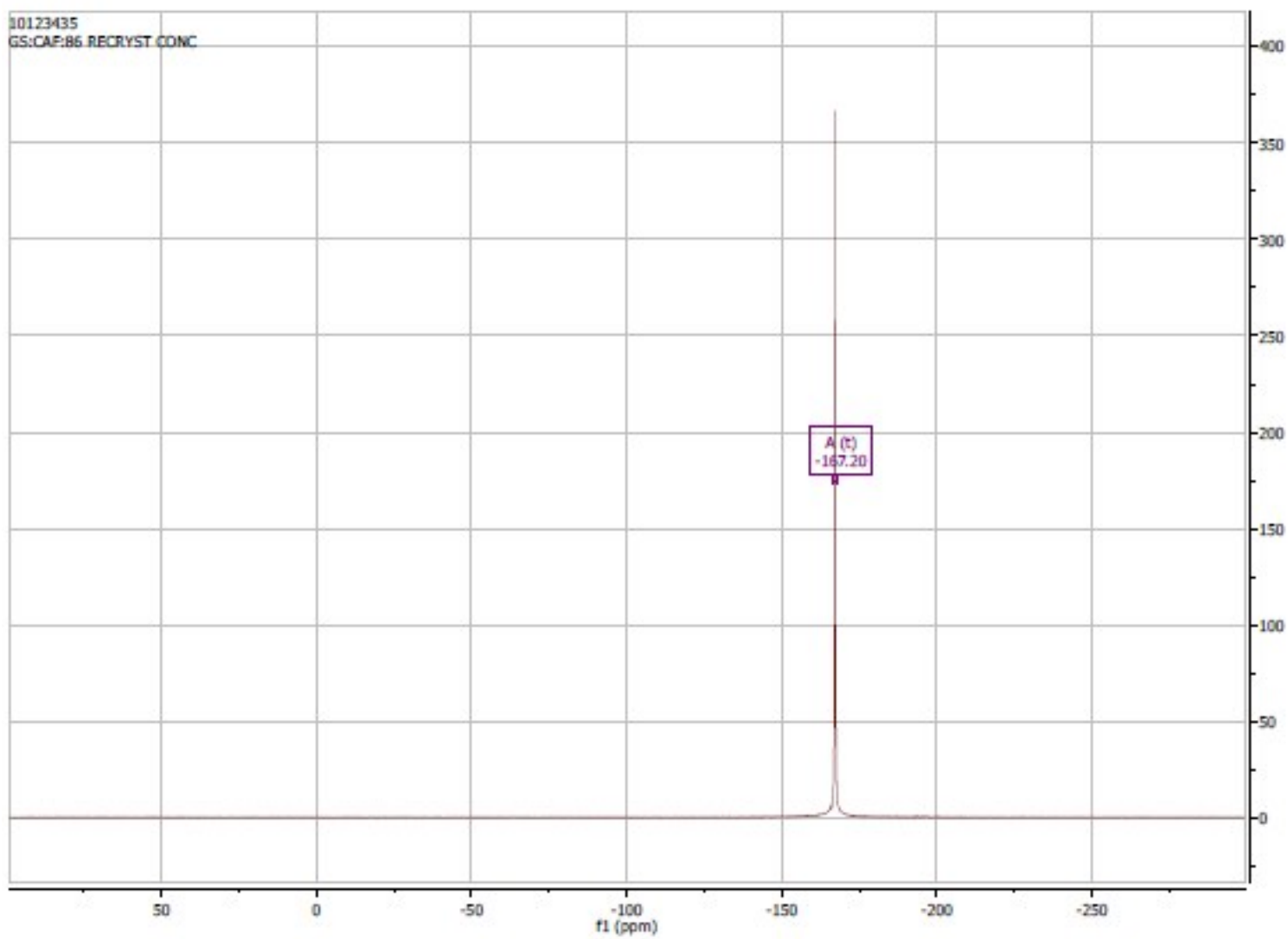
SI-5.2 Dimethyl 2-(3-aminopropyl)-2-fluoromalonate, hydrochloride salt **4c**

^1H NMR spectrum



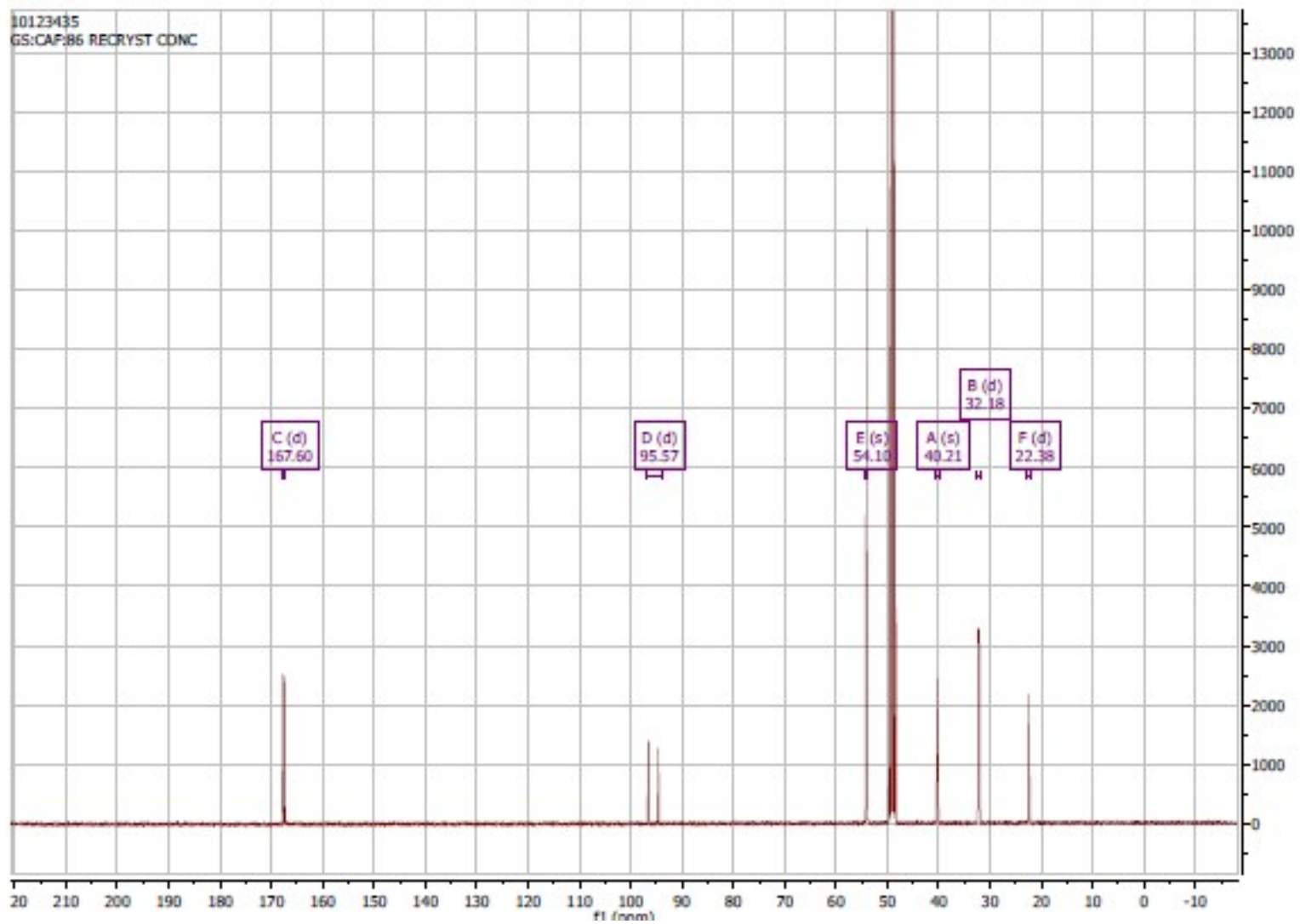
Dimethyl 2-(3-aminopropyl)-2-fluoromalonate, hydrochloride salt **4c**

^{19}F NMR spectrum



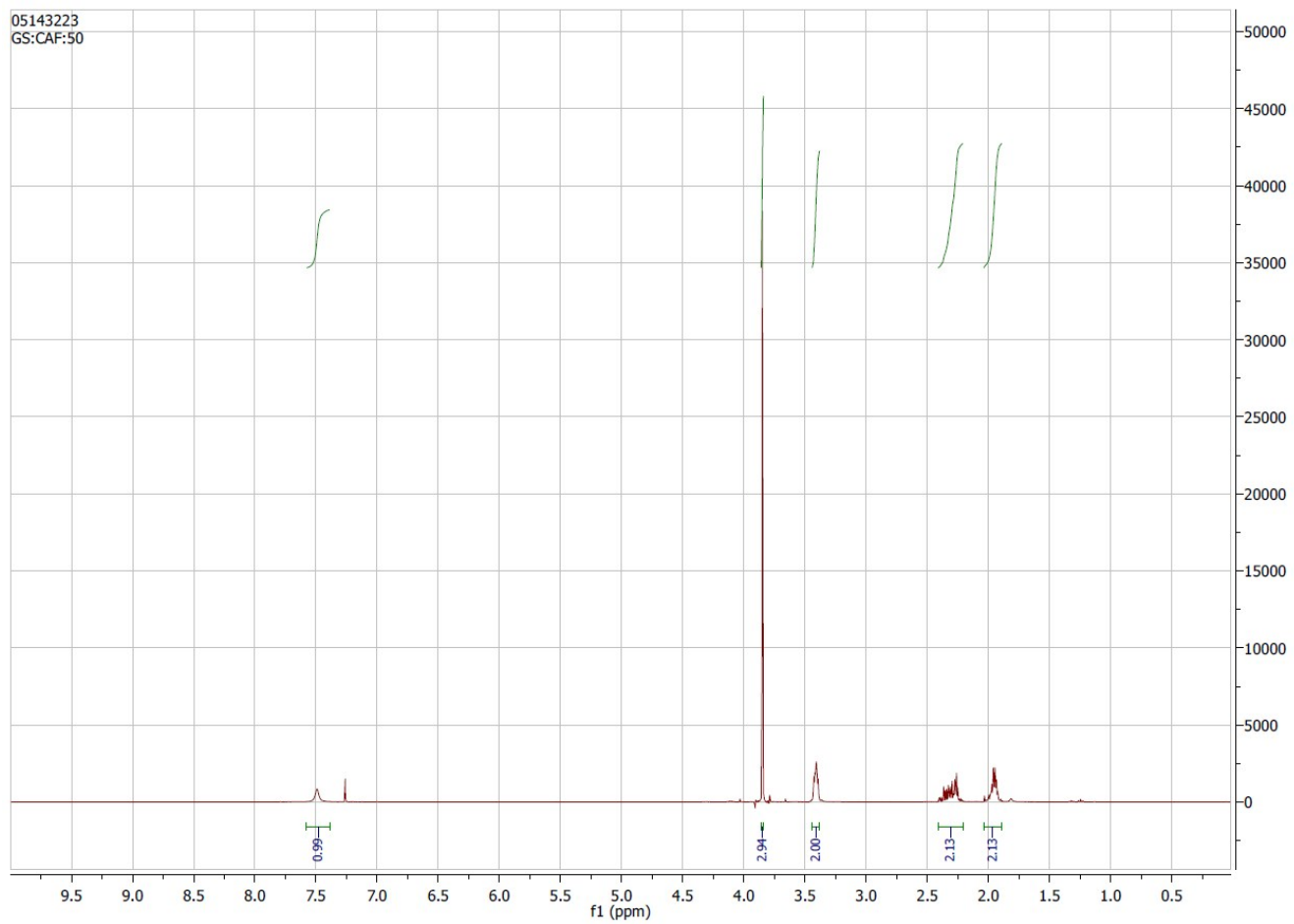
Dimethyl 2-(3-aminopropyl)-2-fluoromalonate, hydrochloride salt **4c**

^{13}C NMR spectrum



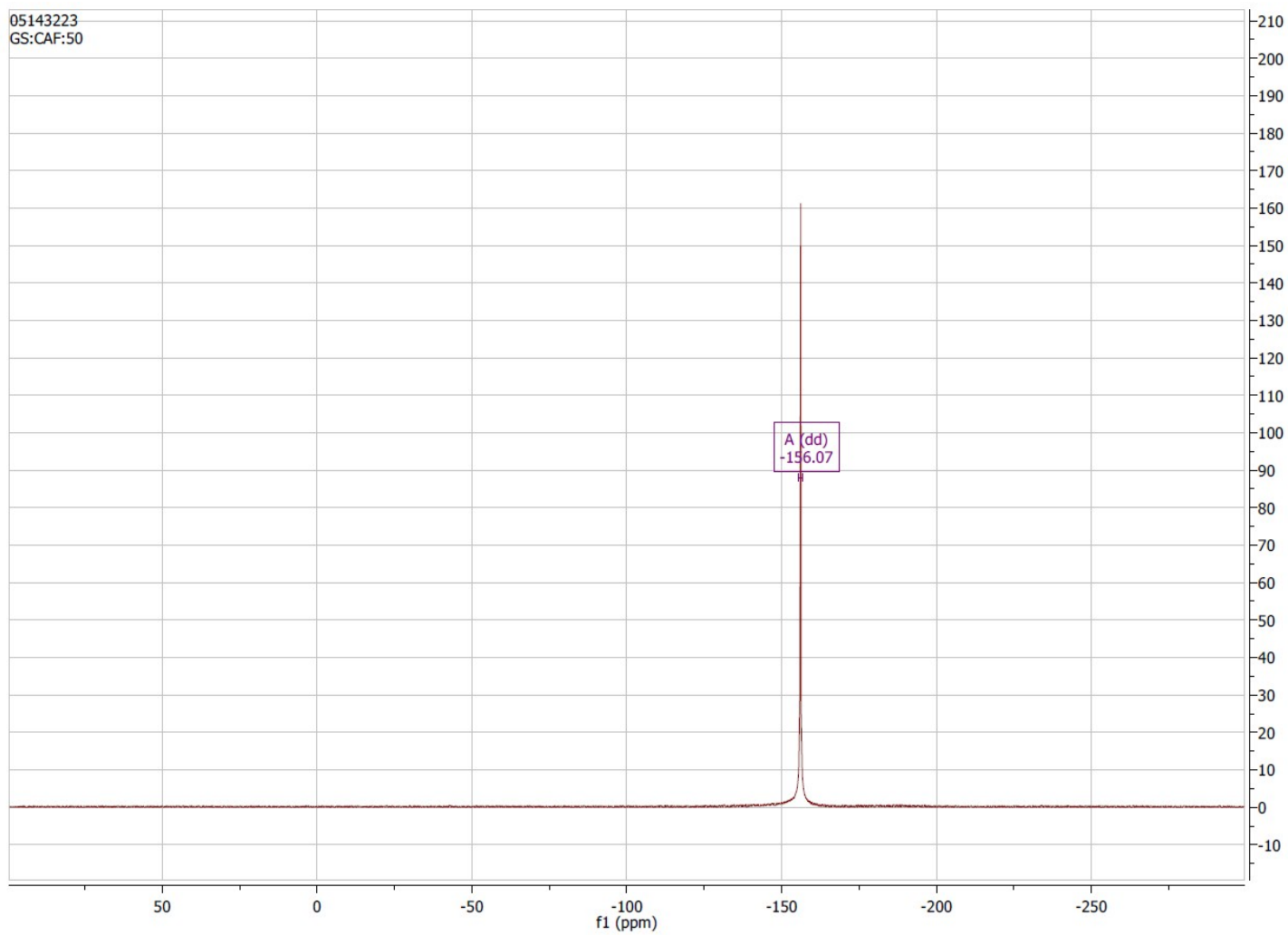
SI-5.3 Methyl 3-fluoro-2-oxo-3-piperidinecarboxylate **4d**

^1H NMR spectrum



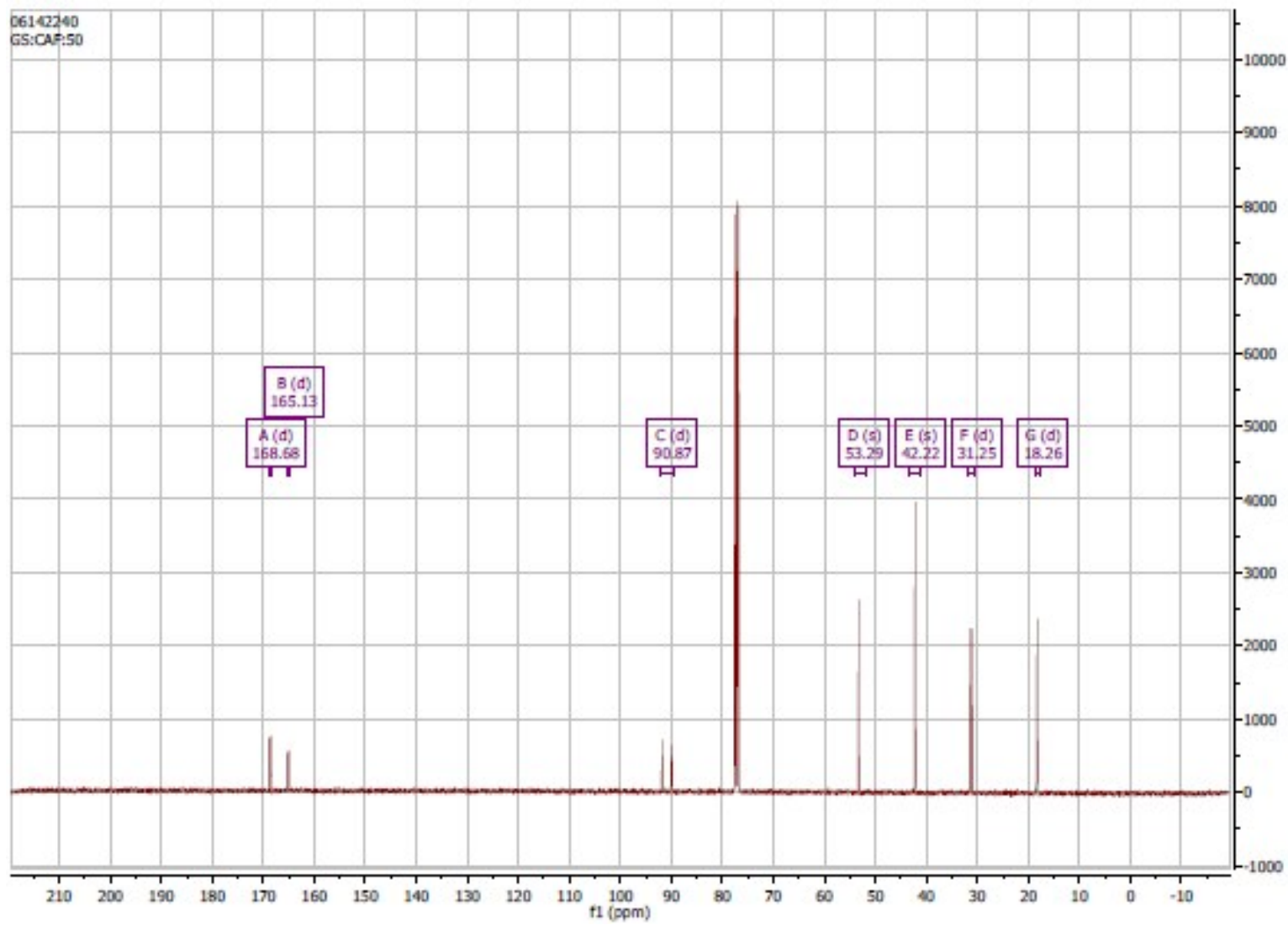
Methyl 3-fluoro-2-oxo-3-piperidinecarboxylate **4d**

^{19}F NMR spectrum



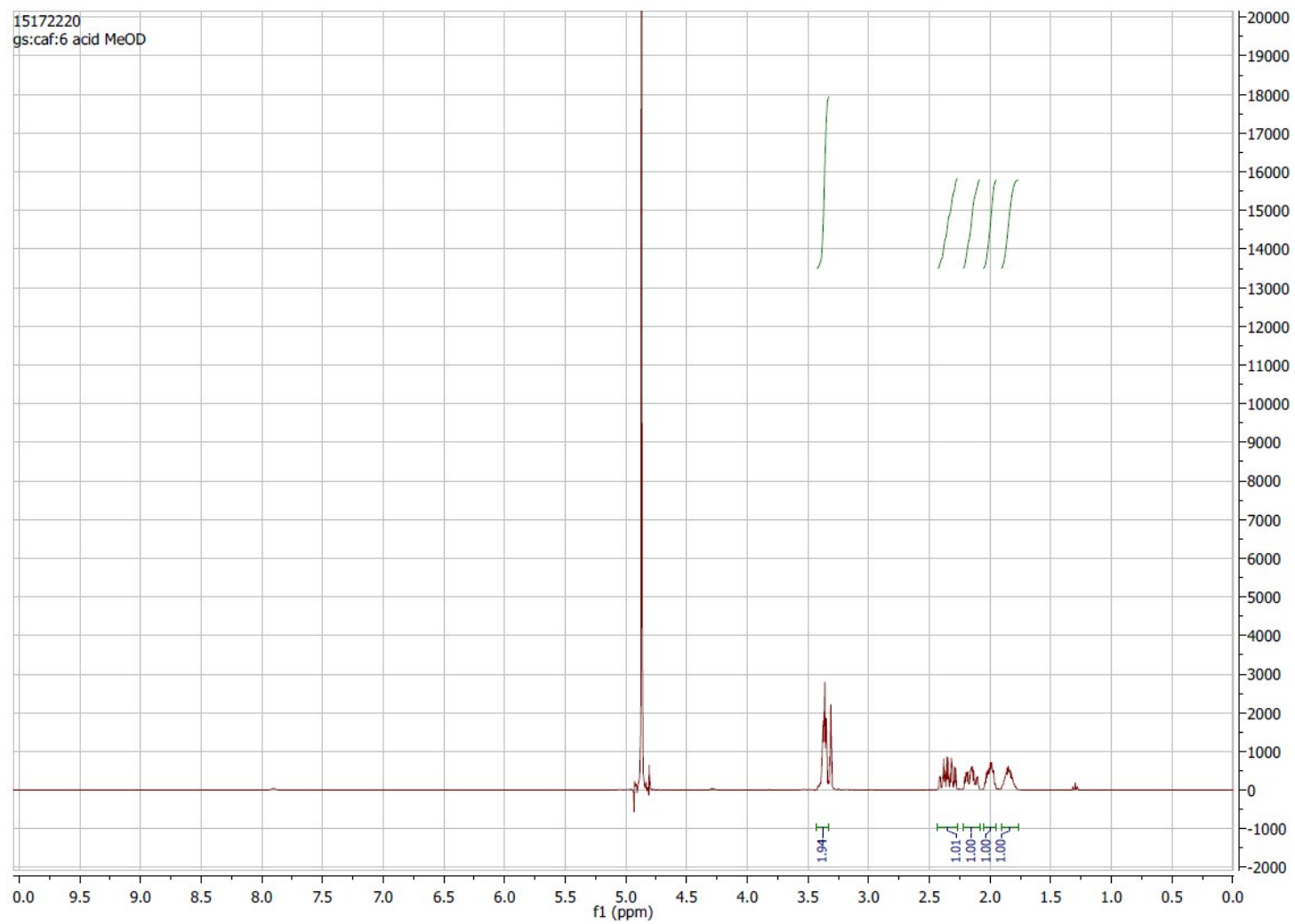
Methyl 3-fluoro-2-oxo-3-piperidinecarboxylate **4d**

^{13}C NMR spectrum



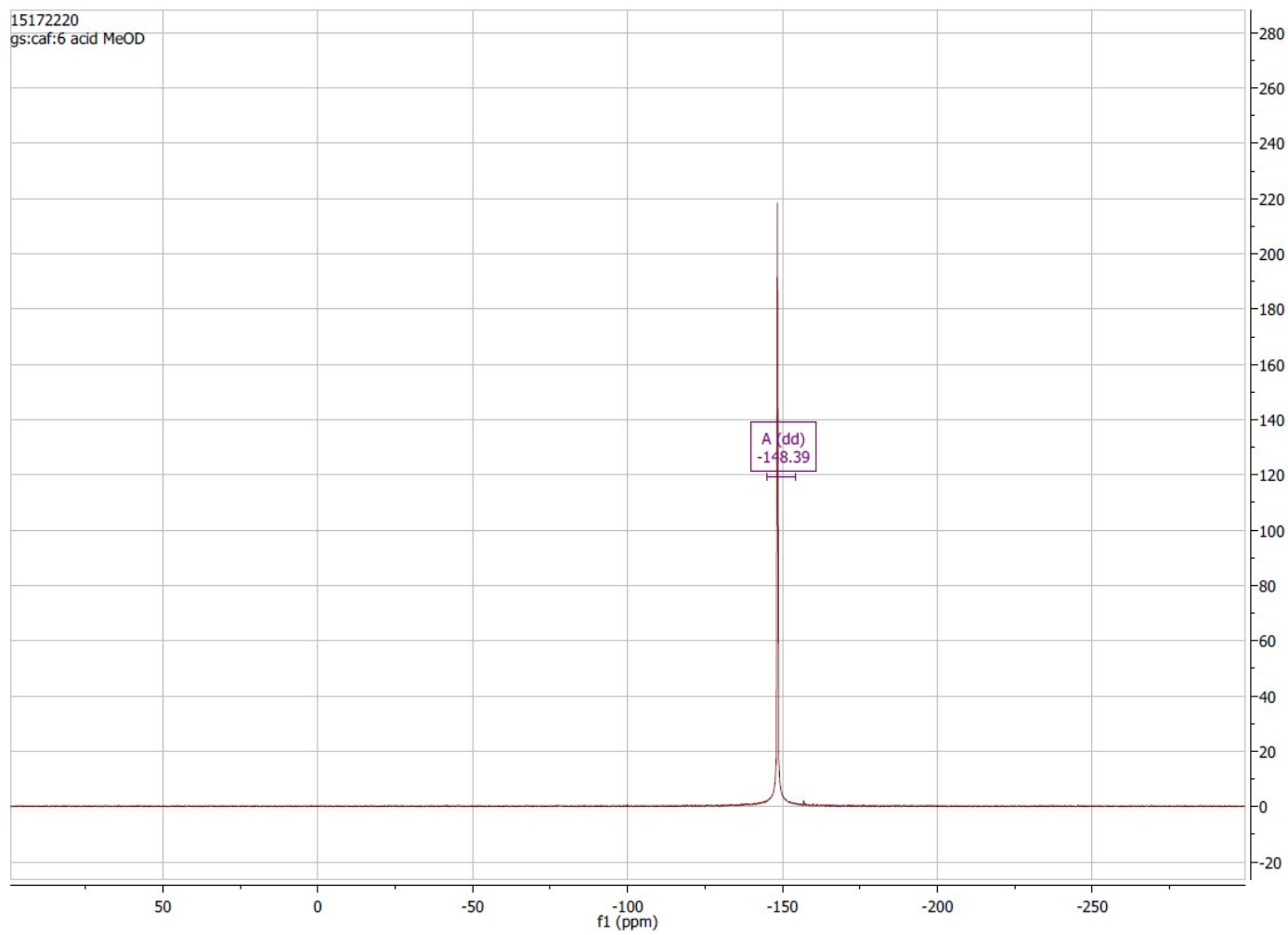
SI-5.4 3-Fluoro-2-oxopiperidine-3-carboxylic acid **5**

^1H NMR spectrum



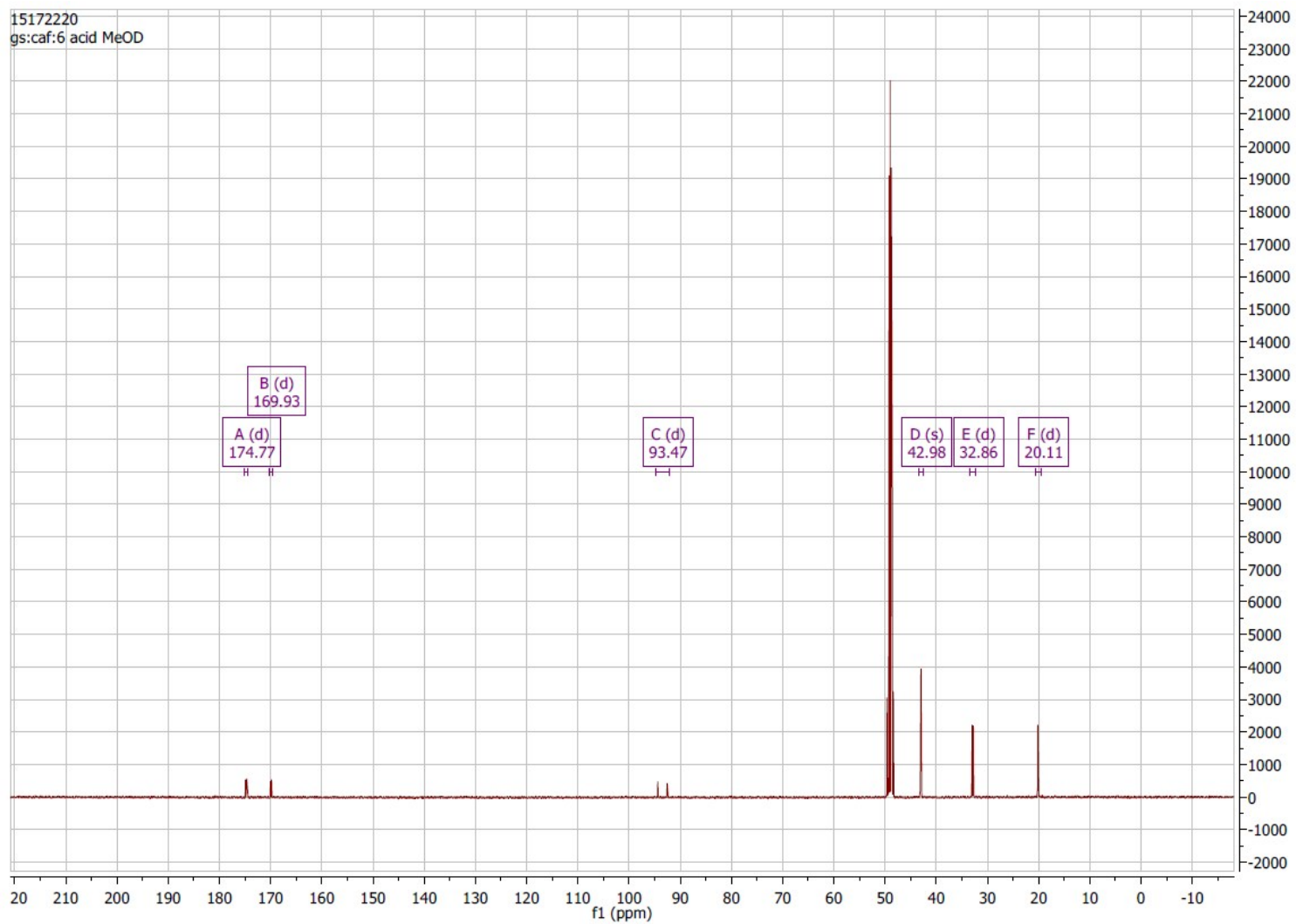
3-Fluoro-2-oxopiperidine-3-carboxylic acid **5**

^{19}F NMR spectrum



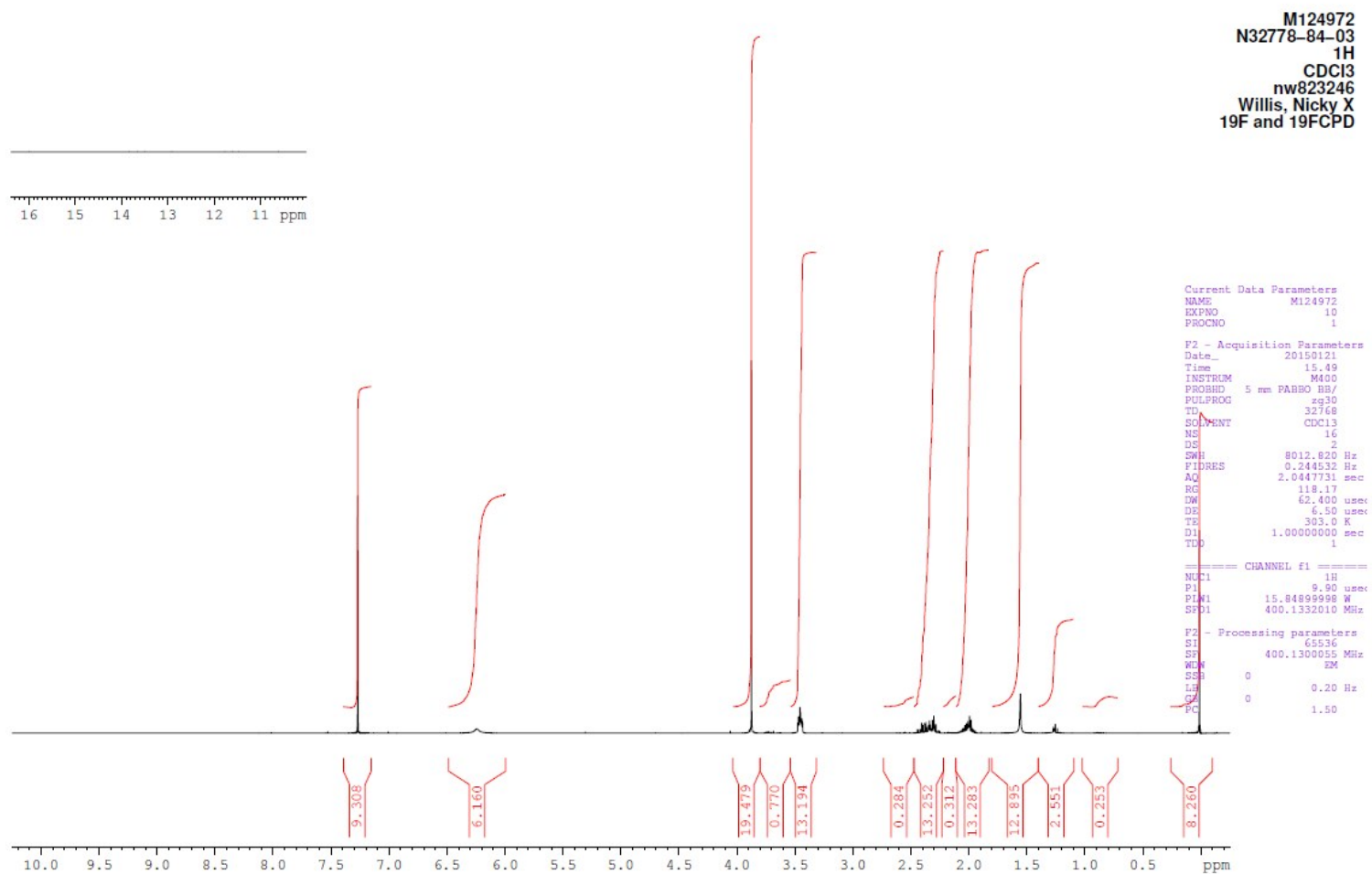
3-Fluoro-2-oxopiperidine-3-carboxylic acid **5**

^{13}C NMR spectrum



SI-5.5 (S)-Methyl 3-fluoro-2-oxopiperidine-3-carboxylate **2b**

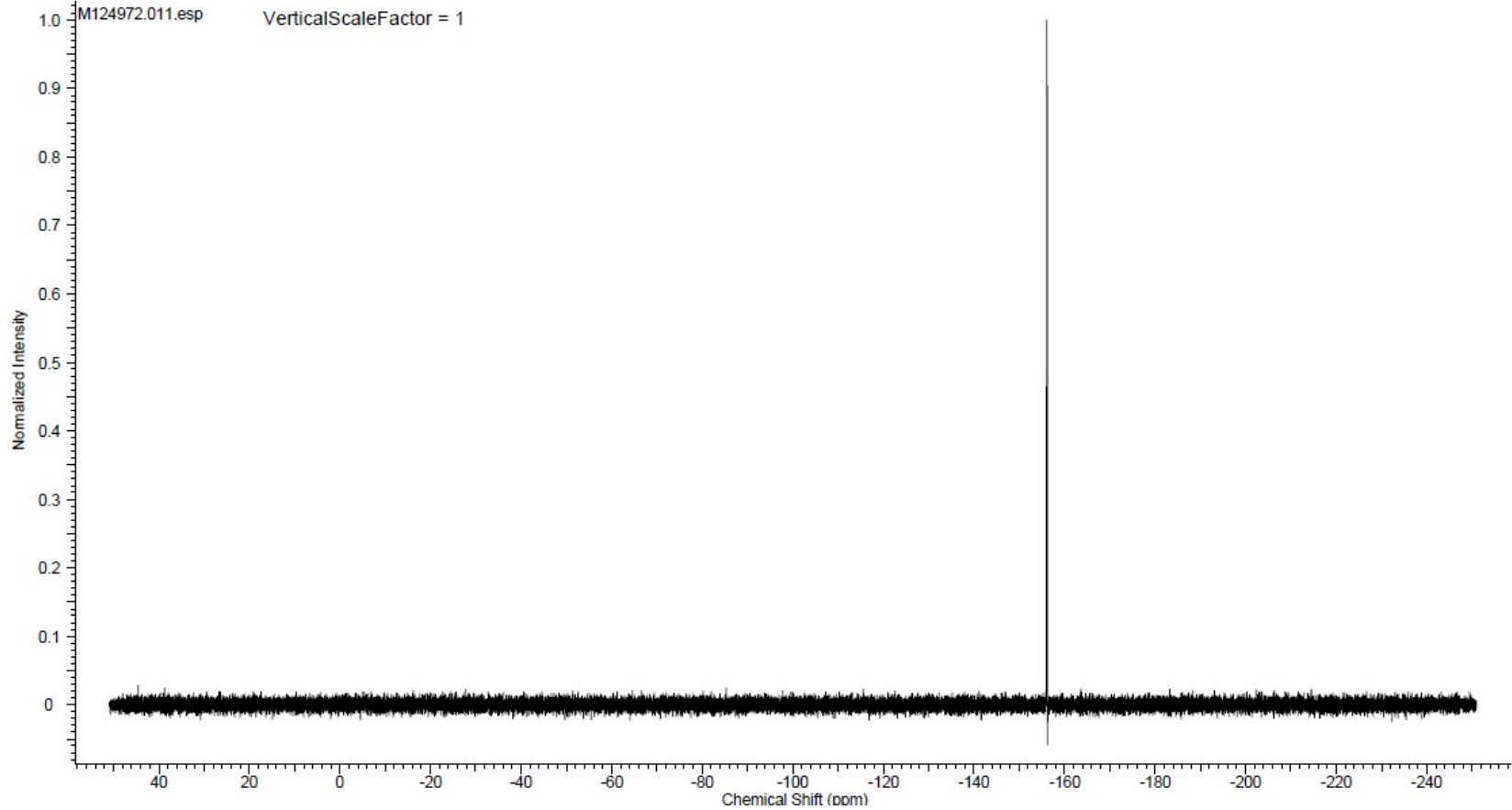
¹H NMR spectrum



(S)-Methyl 3-fluoro-2-oxopiperidine-3-carboxylate **2b**

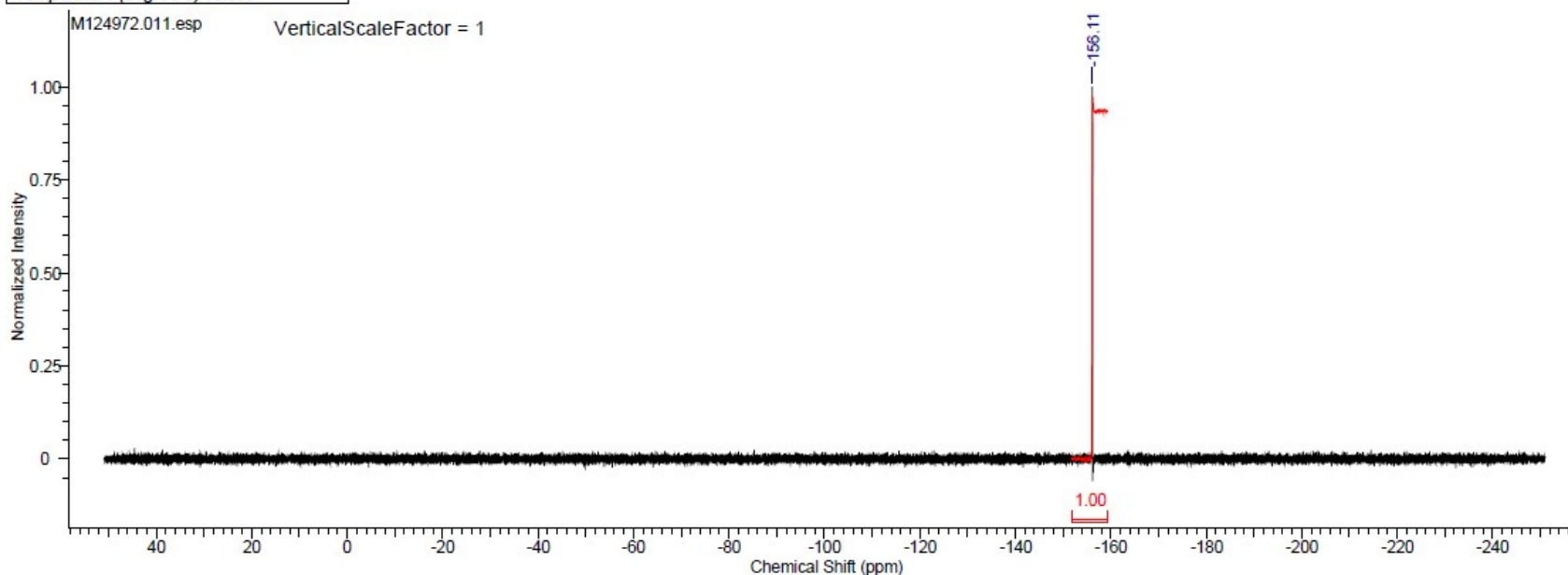
¹⁹F NMR spectrum

Number of Nuclei 0 F's					
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File Name	C:\USERS\CMS26237\APPDATA\LOCAL\TEMP\M124972\11\FID	Frequency (MHz)	376.46	Nucleus	19F
Number of Transients	32	Origin	M400	Original Points Count	32768
Points Count	32768	Pulse Sequence	zg30	Receiver Gain	192.79
Solvent	CHLOROFORM-d	Spectrum Offset (Hz)	-37649.8359	Spectrum Type	STANDARD
Temperature (degree C)	30.005	Sweep Width (Hz)	113632.89		



Number of Nuclei 0 F's

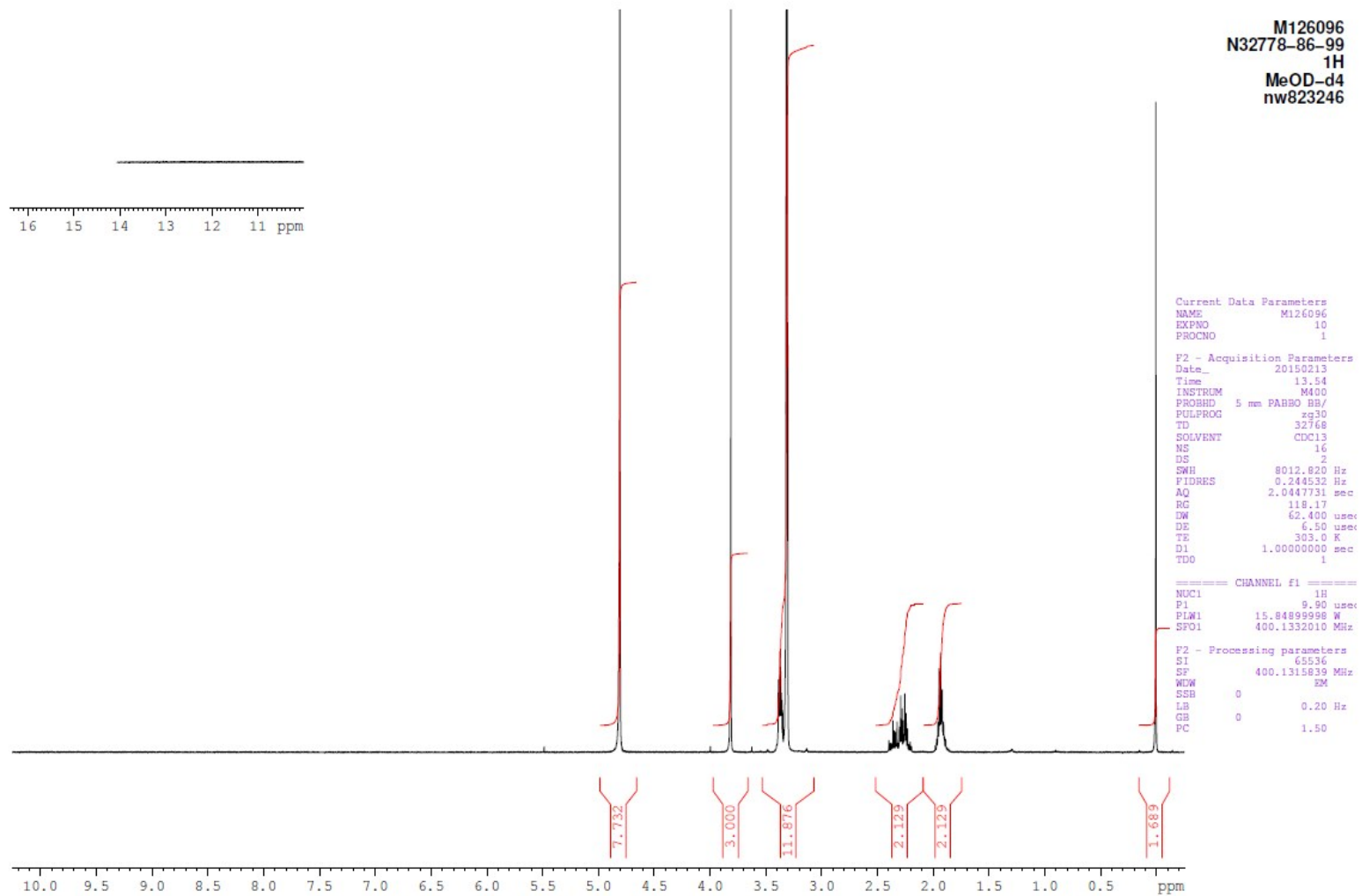
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Date	21 Jan 2015 15:57:52	Date Stamp	21 Jan 2015 15:57:52		
File Name	C:\USERS\CMS26237\APPDATA\LOCAL\TEMP\M124972\11\FID	Frequency (MHz)	376.46	Nucleus	19F
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Temperature (degree C)	30.005			Sweep Width (Hz)	113632.89

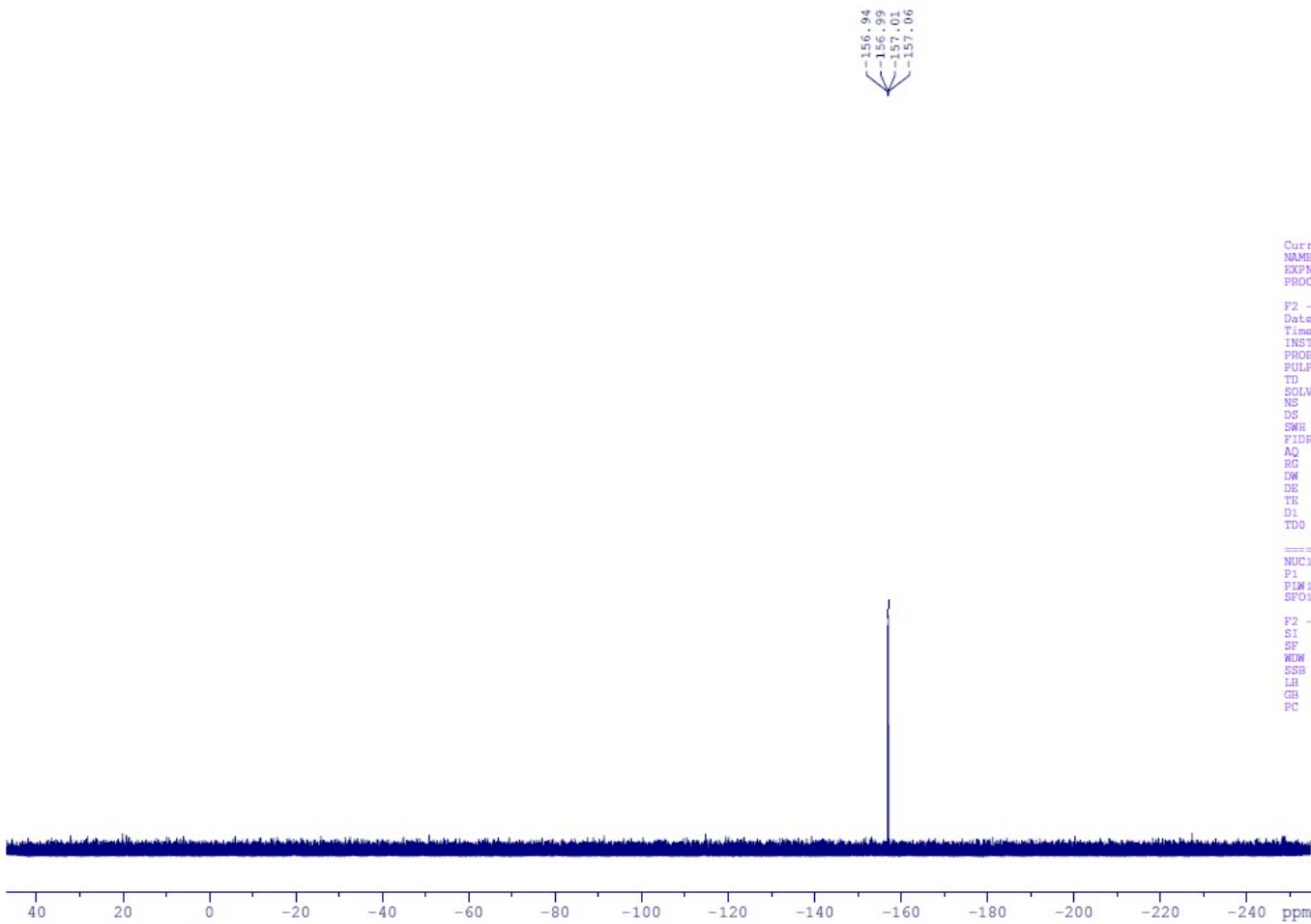


No.	(ppm)	Value	Absolute Value	Non-Negative Value
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No.	(ppm)	(Hz)	Height
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2	-156.12	-58774.6	0.7720
3	-156.11	-58767.7	1.0000
4	-156.06	-58750.3	0.8079

¹H and ¹⁹F NMR spectra of (S)-methyl 3-fluoro-2-oxopiperidine-3-carboxylate **2b** prepared by scaled-up process.





M126096
 N32778-86-99
 19F
 MeOD-d4
 nw823246
 Willis, Nicky X

```

Current Data Parameters
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EXPNO    11
PROCNO    1

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DS         2
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FIDRES     0.216744 Hz
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RG         192.79
DW         4.400 usec
DE         6.50 usec
TE         303.0 K
D1         10.0000000 sec
TDC        1

===== CHANNEL f1 =====
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PLW1       27.98999977 W
SFO1       376.4607162 MHz

F2 - Processing parameters
SI         524288
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